PAT[illegible]T COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 July 2001 (20.07.01)	
International application No. PCT/US00/25155	**Applicant's or agent's file reference** 0887-4147PC1
International filing date (day/month/year) 14 September 2000 (14.09.00)	**Priority date** (day/month/year) 14 September 1999 (14.09.99)
Applicant BARBOUR, Randall, L. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

16 April 2001 (16.04.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland** Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38

0887-4147 PC1
McWha

RECEIVED
DOCKET DEPT.

AUG 2 2 2001

MORGAN & FINNEGAN L.L.P.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

PCT

WRITTEN OPINION

(PCT Rule 66)

	Date of Mailing *(day/month/year)*	17 AUG 2001
Applicant's or agent's file reference 0887-4147PC1	**REPLY DUE** within **TWO** months from the above date of mailing	
International application No. PCT/US00/25155	International filing date *(day/month/year)* 14 SEPTEMBER 2000	Priority date *(day/month/year)* 14 SEPTEMBER 1999
International Patent Classification (IPC) or both national classification and IPC IPC(7): G01N 21/00; H01J 3/14 and US Cl.: 356/436; 250/216		
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK		

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

   I [X] Basis of the opinion

   II [ ] Priority

   III [ ] Non-establishment of opinion with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   DUE: NOVEMBER 17, 2001 PCT Rule 66.2

   V [X] Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [ ] Certain observations on the international application

CASE 0887-4147PC1 ATTY KJM
DUE October 17, 2001 (Written Opinion)
1 mo. call-up September 17, 2001
BY J.M.

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension., see Rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 14 JANUARY 2002

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837 Renee Paxton

Form PCT/IPEA/408 (cover sheet) (July 1998)★

WRITTEN OPINION

International application No.

PCT/US00/25155

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages (See Attached), as originally filed

pages ____________, filed with the demand

pages ____________, filed with the letter of ____________

☒ the claims:

pages (See Attached), as originally filed

pages ____________, as amended (together with any statement) under Article 19

pages ____________, filed with the demand

pages ____________, filed with the letter of ____________

☒ the drawings:

pages (See Attached), as originally filed

pages ____________, filed with the demand

pages ____________, filed with the letter of ____________

☒ the sequence listing part of the description:

pages (See Attached), as originally filed

pages ____________, filed with the demand

pages ____________, filed with the letter of ____________

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language ____________ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*

WRITTEN OPINION	International application No. PCT/US00/25155

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-9, 12, 15-61	YES
	Claims	1, 2, 10, 11, 13, 14	NO
Inventive Step (IS)	Claims	42-50	YES
	Claims	1-41, 51-61	NO
Industrial Applicability (IA)	Claims	1-61	YES
	Claims	NONE	NO

2. citations and explanations

Claims 1, 2, 10-11, and 13-14 lack novelty under PCT Article 33(2) as being anticipated by Swanson et al. (5,459,570). Swanson discloses a source for emitting a signal and having at least one transmitter coupled and a detection system coupled to the energy source and includes at least one energy receiver for measuring dynamic properties of the scattering medium (Abstract & Fig. 1). Swanson further discloses energy transmissive fiber bundle coupled to the energy source and an imaging head for holding the energy transmissive fiber bundle a detection system for collecting data about the optical dynamic properties of the scattering medium.

Claims 3-9, 12, 15-41, and 51-61 lack an inventive step under PCT Article 33(3) as being obvious over Swanson. Applicants claims fail to disclose an inventive step because the modifications are well known in the art and therefore would be obvious to combine with the reference of Swanson.

Claims 42-50 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest an adjustable head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements etc..

Claims 1-41 and 51-61 meet the criteria for industrial applicability set out in PCT Article 33(4), because the present claimed invention is useful in the industry.

ANY RESPONSE MAY BE FAXED TO:
OFFICE OF THE SPECIAL PROGRAM EXAMINER
TECHNOLOGY CENTER 2800
(703) 305-0843

———— NEW CITATIONS ————
US 5,459,570 A (SWANSON et al) 17 October 1995 (17.10.1995), see entire document.

WRITTEN OPINION

International application No.
PCT/US00/25155

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

I. BASIS OF OPINION:

This opinion has been drawn on the basis of the description:
page(s) 1-4, 6-8, 10-14, and 17, as originally filed.
page(s) 5, 9, 15, 16, and 18-27, filed with the demand.
and additional amendments:
NONE

This opinion has been drawn on the basis of the claims:
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) 28-40, filed with the demand.
and additional amendments:
NONE

This opinion has been drawn on the basis of the drawings:
page(s) 1-15, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This opinion has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

PATENT COOPERATION TREATY

0887-4147 PCI

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 59.3(e) and 61.1(b), first sentence and Administrative Instructions, Section 601(a))

Date of mailing (day/month/year) 08 JUN 2001

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
0887-4147PC1	

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US00/25155	14 SEP 00	14 SEP 99

Applicant

THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

16 April 2001

2. That date of receipt is:

- [x] the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- [ ] the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- [ ] the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. [ ] **ATTENTION**: That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

   [ ] *(If applicable)* This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/US	Authorized officer
Assistant Commissioner for Patents Box PCT Washington, D.C. 20231 Attn: IPEA/US Facsimile No.	Diane Russell for Larry Hammond Telephone No. 703 308 6517

Form PCT/IPEA/402 (July 1998)

0887-4147 PC1
Mcwha

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

PCT

NOTIFICATION OF CHANGE IN ABSTRACT AS PREVIOUSLY ESTABLISHED BY INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 38.2(b) and Administrative Instructions, Section 515)

Date of Mailing *(day/month/year)* 14 MAY 2001	
Applicant's or agent's file reference 0887-4147PC1	**INFORMATION ONLY**
International application No. PCT/US00/25155	International filing date *(day/month/year)* 14 SEPTEMBER 2000
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK	

The applicant is hereby notified that this International Search Authority has considered the comments received from the applicant on the abstract established by this Authority (Form PCT/ISA/210) and has decided that:

☐ the text of the abstract remains as previously established by this Authority for the reasons indicated below/in the Annex.

☒ the text of the abstract is changed in view of the applicant's comments and it now reads as it appears below/in the Annex.

Please See Annex to Form PCT/ISA/205.

A copy of this Notification and any Annex has been sent to the International Bureau.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer MICHAEL P. STAFIRA Delmar Perry-Leeper for
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

Form PCT/ISA/205 (January 1994)★

The text of the Abstract as it now reads:

The technical features mentioned in the abstract do not include a reference sign between parentheses (PCT Rule 8.1(d)).

NEW ABSTRACT

A system and method for the detection and three-dimensional imaging of the absorption and scattering properties of a medium, such as human tissue, and the time evolution of these properties, is described. According to one embodiment of the invention, the system directs optical energy toward a turbid medium from at least one source and detects optical energy emerging from the turbid medium as a function of time at a plurality of locations using at least one detector (106). Optical energy emerging from the medium (102) and entering the detector (106) originates from the source (101) and is scattered by the medium (102). The system then generates an image representing interior structure and interior dynamics of the turbid medium based on the detected optical energy emerging from the medium (102). Generating the image includes a time-series measurement and analysis.

0887-4147 PC1
McWha

DOCKET DEPT
2001 JAN 15 P 5:01

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

MORGAN & FINNEGAN LLP

CASE 0887-4147 PC1 ATTY KJM
DUE April 9, 2001 (U.S. Suppl. IDS.)
1 mo. call-up March 9, 2001
BY J.M

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

	Date of Mailing *(day/month/year)* **09 JAN 2001**
Applicant's or agent's file reference 0887-4147PC1	**FOR FURTHER ACTION See paragraphs 1 and 4 below**
International application No. PCT/US00/25155	International filing date *(day/month/year)* 14 SEPTEMBER 2000
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK	

1. [X] The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

CASE 0887-4147PC1 ATTY KJM
DUE March 9, 2001 (Art. 19 Due)
1 mo. call-up 2/9/01
BY J.M

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL P. STAFIRA
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

Form PCT/ISA/220 (July 1998)*

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 0887-4147PC1	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US00/25155	International filing date *(day/month/year)* 14 SEPTEMBER 2000	(Earliest) Priority Date *(day/month/year)* 14 SEPTEMBER 1999
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readable form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (See Box II).

CASE 0887-4147PC1 ATTY KSM

DUE February 9, 2001 (Comments to Abst.)

1 mo. call-up Jan. 24, 2001

BY JM

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 2

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

Form PCT/ISA/210 (first sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/25155

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :G01N 21/00; H01J 3/14
US CL :356/436; 250/216
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/436; 250/216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPTO EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P ---- A	US 5,994,690 A (Kulkarni et al) 30 November 1999, see entire document.	1-3,7,13,14,19 ----- 4-6,8-12,15-18,20-54

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 02 NOVEMBER 2000	Date of mailing of the international search report 09 JAN 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837

NOTES TO FORM PCT/ISA/220 (continued)

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

The statement should be brief, it should not exceed 500 words if in English or if translated into English.

It should not be confounded with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It should not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

In what language ?

The amendments must be made in the language in which the international application is published. The letter and any statement accompanying the amendments must be in the same language as the international application if that language is English or French; otherwise, it must be in English or French, at the choice of the applicant.

Consequence if a demand for international preliminary examination has already been filed ?

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase ?

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;
(ii) the claim is cancelled;
(iii) the claim is new;
(iv) the claim replaces one or more claims as filed;
(v) the claim is the result of the division of a claim as filed.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The technical features mentioned in the abstract do not include a reference sign between parentheses (PCT Rule 8.1(d)).

NEW ABSTRACT

A system and method for the detection and three dimensional imaging of absorption and scattering properties of the medium such as human tissue is described. According to one embodiment of the invention, the system directs optical energy toward a turbid medium from at least one source and detects optical energy emerging from the turbid medium at a plurality of locations using at least one detector (106). The optical energy emerging from the medium (102) and entering the detector (106) originates from the source (101) is scattered by the medium (102). The system then generates an image representing interior structure of the turbid medium based on the detected optical energy emerging from the medium (102). Generating the image includes a time-series analysis.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0887-4147PC1	**FOR FURTHER ACTION** See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/25155	International filing date *(day/month/year)* 14 SEPTEMBER 2000	Priority date *(day/month/year)* 14 SEPTEMBER 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 21/00; H01J 3/14 and US Cl.: 356/436; 250/216		
Applicant THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 27 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 16 APRIL 2001	Date of completion of this report 11 DECEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837 Reece Paustow

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/25155

I. Basis of the report

1. With regard to the **elements** of the international application:*

[ ] the international application as originally filed

[X] the description:
pages (See Attached), as originally filed
pages ________, filed with the demand
pages ________, filed with the letter of ________

[X] the claims:
pages (See Attached), as originally filed
pages ________, as amended (together with any statement) under Article 19
pages ________, filed with the demand
pages ________, filed with the letter of ________

[X] the drawings:
pages (See Attached), as originally filed
pages ________, filed with the demand
pages ________, filed with the letter of ________

[X] the sequence listing part of the description:
pages (See Attached), as originally filed
pages ________, filed with the demand
pages ________, filed with the letter of ________

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language ________ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/ or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25155

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-9, 12, 15-61	YES
	Claims	1, 2, 10, 11, 13, 14	NO
Inventive Step (IS)	Claims	42-50	YES
	Claims	1-41, 51-61	NO
Industrial Applicability (IA)	Claims	1-61	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1, 2, 10-11, and 13-14 lack novelty under PCT Article 33(2) as being anticipated by Swanson et al. (5,459,570). Swanson discloses a source for emitting a signal and having at least one transmitter coupled and a detection system coupled to the energy source and includes at least one energy receiver for measuring dynamic properties of the scattering medium (Abstract & Fig. 1). Swanson further discloses energy transmissive fiber bundle coupled to the energy source and an imaging head for holding the energy transmissive fiber bundle a detection system for collecting data about the optical dynamic properties of the scattering medium.

Claims 3-9, 12, 15-41, and 51-61 lack an inventive step under PCT Article 33(3) as being obvious over Swanson. Applicants claims fail to disclose an inventive step because the modifications are well known in the art and therefore would be obvious to combine with the reference of Swanson.

Claims 42-50 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest an adjustable head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements etc..

Claims 1-41 and 51-61 meet the criteria for industrial applicability set out in PCT Article 33(4), because the present claimed invention is useful in the industry.

------------------- NEW CITATIONS -------------------

US 5,459,570 A (SWANSON et al) 17 October 1995 (17.10.1995), see entire document.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-4, 6-8, 10-14, and 17, as originally filed.
page(s) 5, 9, 15, 16, and 18-27, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) 28-40, filed with the demand.
and additional amendments:
NONE

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page(s) 1-15, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KURT E. RICHTER
MORGAN & FINNEGAN, L.L.P.
345 PARK AVENUE
NEW YORK NY 10154-0053

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)* 31 DEC 2001

Applicant's or agent's file reference
0887-4147PC1

IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US00/25155	14 SEPTEMBER 2000	14 SEPTEMBER 1999

Applicant
THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	MICHAEL P. STAFIRA
Facsimile No. (703) 305-3230	Telephone No. (703) 308-4837

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

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and additional amendments:
NONE

BRIEF DESCRIPTION OF THE FIGURES

For a better understanding of the invention, together with the various features and advantages thereof, reference should be made to the following detailed description of the preferred embodiments and to the accompanying drawings wherein:

FIG. 1 is a block diagram of one embodiment of a system according to the invention;

FIG. 2 is a block diagram illustrating one implementation of the system in FIG. 1;

FIG. 3 is a perspective view of a servo-motor apparatus useful in this invention to illuminate a number of fiber bundles with a single energy source;

FIG. 4 is a schematic illustration of the disposition for examining human tissue such as a human breast;

FIG. 5 is a schematic illustration of a planar imaging head useful in one embodiment of the invention;

FIG. 6 is one embodiment for the source detector arrangement on the imaging head shown in FIG. 5;

FIG. 7 is an illustration of a spherical imaging head useful in practicing the invention;

FIG. 8 is a block diagram of a detector channel useful in practicing the invention;

FIG. 9 is a graphical representation of one implementation of a timing scheme used in the system of FIG.1;

FIG. 10 is a diagram illustrating the sequence of certain events in a multiple channel embodiment of the invention;

displaying the raw data in a color mapping format, features can be extracted by sole visual inspection. In addition to that, analysis algorithms of various types such as, but not limited to, linear and non-linear time-series analysis or pattern recognition methods can be applied to the series of raw data. The advantage of using these analytical methods is the improved capability to reveal dynamic signatures in the signals.

In another implementation, image reconstruction methods may be applied to the sets of raw data thereby providing time series of cross-sectional images of the scattering medium. For these implementations, analysis methods of various types such as, but not limited to, linear and non-linear time-series analysis, filtering, or pattern recognition methods can be applied. The advantage of using such analysis is the improved extraction of dynamic features and cross-sectional view, thereby increasing diagnostic sensitivity and specificity. These methods are explained in detail in the '355 and '322 patents, which were previously described and incorporated in as reference.

The invention reveals measurements of real-time spatiotemporal dynamics. Depending on the implementation, an image of dynamic optical properties of scattering medium such as, but not limited to, the vasculature of the human body in a cross-sectional view is provided. The technology employs low cost, compact instrumentation that uses non-damaging near infrared optical sources and features several alternate imaging heads to permit investigation of a broad range of anatomical sites.

In another implementation, the principles of the present invention can be used in conjunction with contrast agents such as absorbing and fluorescent agents. In another variant, the present invention allows the cross-sectional measurements of changes in

motion protocols such as in a start-stop fashion where the motor stops at a desired location thereby allowing the stable coupling of light into a transmitting fiber bundle. After the measurement at this source location is performed, the motor moves on to the next transmitting fiber. Motion control is in two-way communication with the timing control **104** thereby allowing precise timing of this procedure. Motion control allows the assignment of relative and/or absolute mirror positions allowing for precise alignment of the mirror with respect to the physical location of the fiber bundle. The mirror **306** is surrounded by a cylindrical shroud **309** in order to shield off stray light to prevent cross-talk. The shroud comprises an aperture **310** through which the light beam **302** passes toward the transmitting fiber. It is recognized and incorporated herein other schemes which may be used,(e.g., use of a fiber-optic switching device) to sequentially couple light into the transmitting fibers.

In an equivalent embodiment, fast switching of source positions is accomplished by using a number of light sources, each coupled into one of the transmitting fibers **306** which can be turned on and of each independently by electronic means.

The device employs the servo-motor control system **308** in FIG. 3 with beam steering optics, described above, to sequentially direct optical energy emerging from the source optics onto about 1 mm diameter optical fiber bundles **306**, which are mounted in a circular array in the multiplexing input coupler **300**. The transmitting optical fiber bundles **306**, which are typically 2-3 meters in length are arranged in the form of an umbilical and terminate in the imaging head **206**.

Depending on the implementation, the apparatus of the present invention required for time-series imaging, employs the value of using a geometrically adaptive measurement head or imaging head. The imaging head of the present invention provides features that include, but are not limited to, 1) accommodating different size targets (e.g., breast); 2) stabilizing the target against motion artifacts; 3) conforming the target to well-defined geometry; and 4) to provide exact knowledge of locations for sources and detectors. Stability and a known geometry both contribute to the use of efficient numerical analysis schemes.

There are several different embodiments of the imaging head for data collection that may utilize the principles of the present invention. For example the use of an iris imaging head previously disclosed in the '322 and '355 patents , which are incorporated by reference in this disclosure, may be used with the principles of the present invention.

Described below are two exemplary imaging heads with the understanding that the invention may or may not use any type of imaging head, and if an imaging head is used, it would provide the features previously described.

As illustrated in FIG. 4, the iris unit can be employed as a parallel array of irises **402, 404, 406** enabling volume imaging studies. FIG. 4 illustrates how this can be configured for studying a medium **410**, in this example a human breast, using an imaging head **408**. As described previously, the medium used in the present invention can be any medium, which allows scattering of energy.

In one implementation, the imaging head illustrated in FIG. 5 is a flexible pad configuration. This planar imaging unit functions as a deformable array and is well suited to investigate body structures too large to permit transmission measurements (e.g.,

mm in diameter. Depending on the implementation, eighteen (18) of the sixty-three (63) fiber bundles may be arranged in an array to serve as both optical energy sources or energy transmitters, and receivers to sequentially deliver light to a designated target and receive emerging optical energy. In this implementation, the remaining forty-five (45) fiber bundles act only as receivers of the emerging optical energy.

The geometry of the illumination array is not arbitrary. The design shown in Figure 6 as an exemplary illustration has been configured, as have other implementations, to minimize the subsequent numerical effort required for data analysis while maximizing the source-density covered by the array. The fiber bundles are arranged in an alternating pattern as described by FIG. 6 and shown here with the symbols "X" and "0". In one implementation, a pattern of 00X000X00, X000X000X can be used on the imaging head. 'X' denotes a source/receiver fiber bundle, and '0' is a receiver only. FIG. 6 indicates 2D imaging planes formed by multiple source/detector positions along a line that can be used with this particular pattern. The labels refer to the numbers of sources/detectors found along those lines of optical fiber ends on the pad using the following nomenclature: "S" followed by a number indicates the number of source positions along that line; "D" followed by a number indicates the number of detection points along that line. For instance, "S3-D3" indicates an imaging plane formed by three source positions and three detection points. Basically, the design allows for the independent solution of two dimensional (2-D) image recovery problems from an eighteen (18) point source measurement. As a result, a composite three dimensional (3-D) image can be computed from superposition of the array of 2-D images oriented perpendicular to the target

surface. Another advantage of this geometry is that it readily permits the use of parallel computational strategies without having to consider the entire volume under examination.

The advantage of this geometry is that each reconstruction data set is derived from a single linear array of source-detector fibers, thereby enabling solution of a 2-D problem without imposing undue physical approximations. The number of source-detector fibers belonging to an array can be varied. Scan speeds attainable with the 2-D array illustrated in FIG 6 are the same as for other imaging heads with 2-D arrays since the scan speed depends only on the properties of the input coupler. Thus, faster scan speed are available for the creation of a 3-D image.

In another implementation, illustrated in FIG. 7, is an imaging head based on a "Hoberman" sphere geometry. In a Hoberman structure, the geometry is based on the intersection of a cube and an octahedron, which makes a folding polyhedron called a trapezoidal icosatetrahedron. This structure has been modified and implemented in a form of an imaging head of a hemispherical geometry. For many purposes of the instant invention, it is appropriate to use design features of smoothly varying surfaces based on the Hoberman concept of expanding structures. Depending on the implementation, other polygonal or spherical-type shapes may also be used with the principles of the present invention for other imaging head designs. Adjustment of the device in Figure 7 causes uniform expansion or contraction, thereby always preserving a hemispherical geometry. Imaging head **700** illustrates one example of modification to the "Hoberman" geometry. A receptacle for the fiber bundles **701** is disposed about imaging head **700**. Target volume **702** is where the medium would enter the imaging head in this implementation. This geometry is well suited for the investigation of certain tissues such as the female

breast or the head. Depending on the implementation, attachment of optical fibers to the vertices of the hemisphere allows for up a seventeen (17) source by seventeen (17) detector measurement. The folding structure can be extended to accommodate a more "tear drop" or "bullet" shape of the target medium by attaching additional circular iris-like structures on top that expand and contract with the hemisphere. FIG. 7 shows the combination of the hemisphere with one top iris comprising receptacles for 8 additional fiber bundles leading to an overall number of 25 source by 25 detector positions at the main vertices for this configuration. More than one iris can be attached to the top of the hemisphere. The diameter of the additional top irises may or may not differ from the hemisphere diameter. The detectors or energy receivers may be disposed about the imaging head and the detectors are located on the inner aspect of the expanding imaging head. Additional fiber bundles can be attached to the interlocking joints, permitting up to a 49 source by 49 detector measurement for the hemisphere only and up to 16 source/detector positions per added iris.

Depending on the implementation, light collected from the target medium is measured by using any of a number of optical detection schemes. One embodiment uses a fiber-taper, which is bonded to a charged coupled detector (CCD) array. The front end of the fiber taper serves to receive light exiting from the collection fibers. These fibers are preferably optical fibers, but can be any means that allows the transmission and reception of signals. The back end of the fiber taper is bonded to a 2-D charge-coupled-detector (CCD) array. In practice, use of this approach generally will require an additional signal attenuation module.

An alternate detection scheme employs an array of discrete photo detectors, one for each fiber bundle. This unit can be operated in a phase lock mode thereby allowing for improved rejection of ambient light signals and the discrimination of multiple simultaneously operated energy sources.

In another embodiment, in order to fulfill the demands posed by the desired physiological studies on the instrument, the following features characterize the detector system: scalable multi-channel design (up to 32 detector channels per unit); high detection sensitivity (below 10 pW); large dynamic range ($1{:}10^6$ minimum); multi-wavelength operation; ambient light immunity; and fast data acquisition (order of 100 Hz all-channel simultaneous capture rate).

To achieve this, the detector system uses photodiodes and a signal recovering technique involving electronic gain switching and phase sensitive detection (lock-in amplification) for each detector fiber (in the following referred to as detection or detector channels) to ensure a large dynamic range at the desired data acquisition rate. The phase sensitive signal recovery scheme not only suppresses electronic noise to a desired level but also eliminates disturbances given by background light and allows simultaneous use of more than one energy source. Separation of signals from simultaneously operating sources can be achieved, as long as the different signals are encoded in sufficiently separated modulation frequencies. Since noise reduction techniques are based on the reduction of detection bandwidth, the system is designed to maintain the desired rate of measurements. In order to achieve a timing scheme that allows simultaneous readout of the channels, a sample-and-hold circuit (S/H) is used for each detection channel output. The analog signals provided by the detector channels are sampled, digitized and stored

using the data acquisition system **116**. One aspect is the flexibility and scalability of the detection instrument. Not only are the detector channels organized in single, identical modules, but also the phase detection stages, each containing two lock-in amplifiers, are added as cards. In this way, an existing setup can easily be upgraded in either the number of detector channels and/or the number of wavelengths used (up to four) by cloning parts of the existing hardware.

FIG. 8 shows the block diagram of one implementation of a detector channel. In this implementation , two energy sources are being used. After detecting the light at the optical input **801** by a photo detector **802** the signal is fed to a transimpedance amplifier **803**.(PTA=Programmable Transimpedance Amplifier) The transimpedance value of **803** is externally settable by means of digital signals **813**. This allows the adaptation to various signal levels thereby increasing the dynamic range of the detector channel. The signal is subsequently amplified by a Programmable Gain Amplifier (PGA) **804** whose gain can be set externally by means of digital signals **814**. This allows for additional gain for the lowest signal levels (e.g., in one implementation ~pW-nW) thereby increasing the dynamic range of the detector channel.

In one embodiment, at least one energy source is used and the signal is sent to at least one of lock-in amplifiers (LIA) **805, 809**. Each lock-in amplifier comprises an input **808,812** for the reference signal generated by phase shifter **204** from FIG 2. After lock-in detection, the demodulated signal is appropriately boosted in gain by means of a programmable gain amplifier (PGA) **806, 810** in order to maximize noise immunity during further signal transmission and to improve digital resolution when being digitized. The gain of PGA **806, 810** is set by digital signals **815**.

At each output, a sample-and-hold circuit (S/H) **807, 811** is used for freezing the signal under digital timing by means of signal **816** for purposes described herein.

In one embodiment, the signal **815** is sent to **806, 810** in parallel. In one embodiment, the signal **816** is sent to **807, 811** in parallel.

As previously illustrated in FIG. 1, the analog signal provided by each of the channel outputs is sampled a data acquisition system **116**. In one embodiment, PC extension boards might be used for this purpose. PC extension boards also provide the digital outputs that control the timing of functions such as gain settings and sample-and-hold.

As previously noted, timing is crucial in order to provide the desired image capture rate and to avoid false readings due to detector-to-detector time skew. FIG. 9 shows one improvement of the invention over other timing schemes. With systems not comprising fast adaptable gain settings (such as some CCD based systems), a schedule according to **905** has to be implemented. A time series of data is acquired for a fixed source position. After finishing this task, the source is being moved **902** with respect to the target **901** and another series of data is being collected. Measurements are being performed in this fashion for all source positions. Every image **903** of the resulting time series of reconstructed images are being reconstructed from data sets merged together from the data for each source position. This schedule does not allow real-time capture of all physiologic processes in the medium and therefore only applies to certain modes of investigation. Although we are aware of the use of such schemes, e.g., when monitoring responses on repeatable maneuvers, the timing scheme for the invention very much improves on this situation.

Because the invention allows for fast source switching and large dynamic range and high data acquisition rates, a schedule indicated by **904** is performed. Here, the source position is switched fast compared to the dynamic features of interest and instantaneous multi-channel detection is performed at each source position. Images **903** are then reconstructed from data sets, which represent an instant state of the dynamic properties of the medium. Only one time series of full data sets (i.e., all source positions and all detector positions) is being recorded. Real time measurement of fast dynamics (e.g., faster 1 Hz) of the medium is provided by the invention. The implementation in FIG 9 illustrates one use of a silicon photo-diode in process **904**, which can be replaced by various detectors previously mentioned.

FIG 10 shows one embodiment of a detailed schedule and sequence of the system tasks **1001** involved in collecting data at a source position and the proceeding of this process in time **1002**. Task **1003** is the setting of the optical de-multiplexer to a destined source position and setting the detectors to the appropriate gain settings. The source position is illuminated for a period of time **1004**, during which the lock-in amplifiers settle **1005**. After the time it takes the S/H to sample the signal **1006**, the signal is being hold for a period of time **1007**, during which all channels are being read pout by the data acquisition. It is worthwhile noticing that during reading out the S/H, other tasks, like moving the optical source, setting the detector gains for the new source position, and settling of the lock-in, are being scheduled. This increases greatly the achievable data acquisition rate of the instrument.

This concept of a modular system is further illustrated in FIG. 11. Up to thirty-two (32) detector modules **1100** (each with 2 lock-in modules each for two modulation

frequencies) are arranged using an enclosure **1102**. The cabinet also can carry up to two phase shifting modules **1104**, **1106**, each containing two digital phase shifter under computer control. The ability to adjust the reference phase with respect to the signal becomes necessary since unavoidable phase shifts in the signal may lead to non-optimum lock-in detection or can even result in a vanishing output signal. Organization of data, power supply and signal lines is provided by means of two back planes **1108**, **1110**

Depending on the implementation, the detector system design illustrated in FIG. 8 allows one cabinet to operate at a capacity of 32 detectors with four different sources requiring 128 analog to digital circuit (ADC)-board input channels. The upper **1108** and the lower **1110** back plane are of identical layout and have to be linked in order to provide the appropriate distribution of supply-, control- and signal voltages. This is achieved using a 6U-module fitting both planes from the backside, that provides the necessary electric linking paths, and interfaces for control- and signal lines.

FIG. 12 shows the schematic of one implementation of a channel module. In this implementation, a silicon photodiode 1206 is used as the photo-detector. A Programmable Transimpedance Amplifier (PTA) **1201** is formed by an operational amplifier **1204** , resistors **1201** and **1202** and an electronic switch **1205**, the latter of which is realized using a miniature relay. Other forms of electronic switches such as analog switches might be used. Relay **1205** is used to connect or disconnect 1203 from the circuit thereby changing the transimpedance value of **1201**. A high-pass filter (R2, C5) is used to AC-couple the subsequent programmable gain instrumentation amplifier **IC2** (Burr Brown PGA202) in order to remove DC offset. The board-to-board connectors

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for the two lock-in-modules are labeled as "slot A" **1210** and "slot B" **1212**. The main connector to the backplane is a 96-pole DIN plug **1220**.

FIG. 13, illustrates the electric circuit of the lock in modules **1210, 1212**. The signal is subdivided and passed to two identical lock-in-amplifiers, each of which gets one particular reference signal according to the sources used in the experiment. The signal is first buffered **IC1, IC7** (AD LF111) and then demodulated using an AD630 double-balanced mixer **IC2, IC8**.

In order to remove undesired AC components, the demodulated signal passes through an active 4-pole Bessel-type filter **IC3, IC4, IC 9, IC10** (Burr Brown UAF42). A Bessel-type filter has been chosen in order to provide fastest settling of the lock-in amplifier for a given bandwidth. Since a Bessel-filter shows only slow stopband-transition, a 4-pole filter is being used to guarantee sufficient suppression of cross talk between signals generated by different sources (i.e. of different modulation frequency). The filter has its 3 dB point at 140 Hz, resulting in 6 ms settling time for a step response (<1% deviation of actual value). The isolation of frequencies separated by 1 kHz is 54 dB. The filters are followed by a programmable gain amplifier **IC5, IC 11**, whose general function has been described above. The last stage is formed by a sample-and-hold chip (S/H) **IC6, IC12** (National LF398).

In another implementation, the phase sensitive detection can be achieved with digital methods using digital signal processing (DSP) components and algorithms. The advantage of using DSP with the principles of the present invention is improved electronic performance and enhanced system flexibility.

In another implementation, an analog-to-digital converter is used for each detector channel thereby improving noise immunity of the signals.

Although illustrative embodiments have been described herein in detail, those skilled in the art will appreciate that variations may be made without departing from the spirit and scope of this invention. Moreover, unless otherwise specifically stated, the terms and expressions used herein are terms of description and not terms of limitation, and are not intended to exclude any equivalents of the system and methods set forth in the following claims.

What is claimed is:

1. A system for use in tomographic imaging of a scattering medium, comprising:

an energy source for emitting a signal and having at least one energy transmitter coupled thereto; and

a detection system coupled to the energy source and including at least one energy receiver for measuring dynamic properties of the scattering medium.

2. The system of claim 1, further including an imaging head coupled as the energy transmitter and energy receiver for holding thereof.

3. The system of claim 1, wherein the detection system further comprises at least one lock-in amplifier for separating a signal emitted by at least one energy source.

4. The system of claim 1, wherein the detection system further includes at least one gain adjustment means for increasing dynamic range of the detector system.

5. The system of claim 1, wherein the detection system further includes a sample-and-hold circuit for freezing the signal emitted by the energy source.

6. The system of claim 5, wherein the sample-and-hold circuit further includes logic for allowing simultaneous readout for each detector fiber.

7. The system of clam 1, wherein the energy source includes at lest one of non-laser optical sources, LED and high-pressure incandescent lamp, laser diodes, solid state lasers, titanium-sapphire laser, ruby laser, dye laser, electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and combinations thereof.

8. The system of claim 1, wherein data acquisition from the detection system is about 150Hz.

9. The system of claim 1, wherein the energy source includes a plurality of near infra red laser diodes to transmit multiple wavelengths.

10. A detection system to collect data about the dynamic properties of a scattering medium, comprising:

at least one energy receiver for detecting a signal from an energy source; and

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a programmable gain instrumentation amplifier for increasing the dynamic range of the signal which provides rapid data acquisition about the dynamic properties of the scattering medium.

11. The detection system of claim 10, wherein the energy receiver includes at least one of a photo-diode, PIN diode, Avalanche photodiodes , change couple device, change inductive device, photo-multiplier tubes, multi-channel plate, acoustic transducers, and any combinations thereof.

12. The detection system of claim 10, further including a sample-and-hold circuit coupled to the programmable gain instrumentation amplifier that allows simultaneous readout of a plurality of signals from the energy source.

13. A system for use in optical tomographic imaging of a scattering medium comprising:

at least one energy transmissive fiber bundle coupled to an energy source;

an imaging head for holding the energy transmissive fiber bundle; and

a detection system for collecting data about the optical dynamic properties of the scattering medium.

14. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

15. The system of claim 13, wherein the fiber bundle only transmits energy.

16. The system of claim 13, wherein the imaging head is a folding sphere or polygon.

17. The system of claim 16, wherein the polygon is a polyhedron or a trapezoidal icosatetrahedron, or a hemitrapezoidal icosatetrahedron..

18. The system of claim 16, wherein the fiber bundle is disposed about the imaging head.

19. The system of claim 13 wherein the fiber bundle has a diameter of about 3 mm.

20. The system of claim 13, wherein the imaging head further includes adjustment means for accommodating different size medium, stabilizing the medium against motion artifacts, conforming the target to a simple well-defined geometry and

providing information about the location of at lest the receiver in reference to the location of the transmitter.

21. A method of using optical tomographic imaging, comprising:

(a) exposing a scattering medium to near infra-red light; for collecting data about the dynamic properties of a scattering medium,

(b) detecting light by a detection system; and

(c) enhancing gain through a programmable gain instrumentation amplifier for the purpose of measuring the dynamic properties of the scattering medium.

22. The method of claim 21, wherein the scattering medium is vascular tissues.

23. The method of claim 21, further including separating via at least one lock-in amplifier a plurality of wavelengths transmitted through the medium.

24. The method of claim 21, further including collecting data from simultaneous readouts of a signal.

25. A system for optical tomographic imaging of a medium comprising:

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an imaging head having at least one source disposed to direct optical energy into a medium and a plurality of detectors disposed to receive optical energy emerging from the medium, the detectors means being located at a plurality of distances from the source constituting a plurality of distances through the medium the detectors and thee source , the source and detectors forming respective source detector pairs;

a programmable gain amplifier connected to amplify at least one signal of the source detector pairs;

a computer having a data acquisition board for receiving the signal from the programmable gain amplifier and reconstructing an image of the medium.

26. The system of claim 25, wherein the optical energy comprises optical energy of at least two different intensity modulated wavelengths of energy.

27. The system of claim 26, further comprising a filtering means for separating signals corresponding to a wavelength of intensity modulated energy.

28. The system of claim 25, further comprising a sample and hold circuit for holding a desired signal for use in measuring of dynamic properties of the medium.

29. The system of claim 25, wherein the source comprises energy transmissive fibers coupled to an energy emitting source.

30. The system of claim 25, wherein the source comprises a plurality of optical energy sources.

31. The system of claim 25, wherein the source comprises of plurality of laser diodes.

32. The system of claim 25, wherein the detectors are fibers coupled to optical energy detectors.

33. The system of claim 25, wherein the detectors are optical energy detectors.

34. An imaging head comprising

a pad;

a plurality of source means for delivering optical energy to a medium; and

a plurality of detector means for detecting optical energy emerging from a medium, the source means and detector means being attached to the pad in a plurality of rows and columns wherein the plurality of source means are arranged to form at least two unique imaging planes, an imaging plane being between defined by a plane substantially perpendicular to the pad and passing through at least two source means and one detector means.

35. The imaging head of claim 34, wherein a plurality of source means and detector means are joined to form combined source detector means, the combined source detector means and detector means being arranged in an alternating rows of a first pattern and a second pattern, the first pattern comprising one combined source detector means followed by three detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means, the second pattern comprising two detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means followed by two detector means.

36. The imaging head of claim 34, wherein the source means are fibers coupled to an optical energy source.

37. The imaging head of claim 34, wherein the source means are optical energy sources.

38. The imaging head of claim 34, wherein the source means is laser diodes.

39. The imaging head of claim 34, wherein the detector means are fibers coupled to optical energy detectors.

40. The imaging head of claim 34 wherein the detector means are optical energy detectors.

41. The imaging head of claim 34 wherein the detector means are photodiodes.

42. An adjustable imaging head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements, each trust element having a central pivot point, an internal terminal pivot point and an external terminal pivot point that do not lie on a straight line, each strut being pivotally joined to the other of its pair by their central pivot points, each strut being pivotally joined by the internal terminal pivot point and the external terminal pivot point to the internal terminal pivot point and the external terminal pivot point respectively of another scissors pair, whereby an adjustable ring of principle vertices is formed by the internal terminal pivot points and whereby adjustment causes uniform movement of the principle vertices, the improvement comprising:

at least one source means for delivering optical energy into a medium and at least one detector means for detecting optical energy emerging from a medium, wherein the source means and the detector means are attached to the principle vertices, the source means being oriented to direct optical energy substantially toward a medium in

the center of the ring, the detector means being oriented to receive optical energy emerging substantially from a medium in the center of the ring.

43. The adjustable imaging head of claim 42, further comprising:

amount in communication with a truss element, wherein the mount supports the imaging head and regulates the size of the adjustable ring.

44. The adjustable imaging head of claim 42, further comprising:

a first set of mounts in communication with a first set of diametrically opposed external terminal pivot points;

a second set of mounts in communication with a second set of diametrically opposed external terminal pivot points, wherein the first set of diametrically opposed external terminal pivot points is orthogonal to the second set of diametrically opposed external terminal pivot points,

a drive system in communication with at least one of the mounts in at least one of the first or second sets of mounts, whereby the drive system regulates the size of the adjustable ring.

45. The imaging head of claim 42, wherein the source means are fibers coupled to an optical energy source.

46. The imaging head of claim 42, wherein the source means are optical energy sources.

47. The imaging head of claim 42, wherein the source means are laser diodes.

48. The imaging head of claim 42, wherein the detector means are fibers coupled to optical energy detectors.

49. The imaging head of claim 42, wherein the detector means are optical energy detectors.

50. The imaging head of claim 42, wherein the detector means are photodiodes.

51. An imaging head for use in optical tomography, comprising:

at least one energy receiver;

adjustment means for accommodating different sizes of the medium; and

communication means for transmitting signals from the imaging head to a detection system for use in the measurement of dynamic properties of a scattering medium.

52. The imaging head of claim 49, further including at least one energy transmitter.

53. The imaging head of claim 52, wherein the energy transmitters define an illumination array configured to minimize subsequent numerical effort required for data analysis and maximizing source density covered by the array.

54. The imaging head of claim 53, wherein three dimensional images can be computed from super positioning of the array of two dimensional images.

55. The detection system of claim 10, wherein the energy receiver further detects fluorescence radiation excited by the energy source.

56. The detection system of claim 10, wherein the energy receiver further detects acoustic energy produced in the scattering medium by an optical source.

57. The system of claim 13, wherein the fiber bundle only detects energy.

58. The system of claim 13, wherein the transmissive fiber bundle terminates inside the scattering medium.

59. The method of claim 21, further including the step of evaluating the dynamics in an industrial mixing process for materials selected from the group consisting of powder, gas, liquid, porous material, and combinations thereof.

60. The method of claim 21, further including the step of evaluating dynamics in foggy atmospheres for meteorology.

61. The method of claim 21, further including the step of evaluating dynamics in oceans or water masses.

BRIEF DESCRIPTION OF THE FIGURES

For a better understanding of the invention, together with the various features and advantages thereof, reference should be made to the following detailed description of the preferred embodiments and to the accompanying drawings wherein:

FIG. 1 is a block diagram of one embodiment of a system according to the invention;

FIG. 2 is a block diagram illustrating one implementation of the system in FIG. 1;

FIG. 3 is a perspective view of a servo-motor apparatus useful in this invention to illuminate a number of fiber bundles with a single energy source;

FIG. 4 is a schematic illustration of the disposition for examining human tissue such as a human breast;

FIG. 5 is a photograph of a planar imaging head useful in one embodiment of the invention;

FIG. 6 is one embodiment for the source detector arrangement on the imaging head shown in FIG. 5;

FIG. 7 is an illustration of a spherical imaging head useful in practicing the invention;

FIG. 8 is a block diagram of a detector channel useful in practicing the invention;

FIG. 9 is a graphical representation of one implementation of a timing scheme used in the system of FIG.1;

FIG. 10 is a diagram illustrating the sequence of certain events in a multiple channel embodiment of the invention;

displaying the raw data in a color mapping format, features can be extracted by sole visual inspection. In addition to that, analysis algorithms of various types such as, but not limited to, linear and non-linear time-series analysis or pattern recognition methods can be applied to the series of raw data. The advantage of using these analytical methods is the improved capability to reveal dynamic signatures in the signals.

In another implementation, image reconstruction methods may be applied to the sets of raw data thereby providing time series of cross-sectional images of the scattering medium. For these implementations, analysis methods of various types such as, but not limited to, linear and non-linear time-series analysis, filtering, or pattern recognition methods can be applied. The advantage of using such analysis is the improved extraction of dynamic features and cross-sectional view, thereby increasing diagnostic sensitivity and specificity. These methods are explained in detail in the '355 and '322 patents, which were previously described and incorporated in as reference.

The invention reveals measurements of real-time spatial temporal dynamics. Depending on the implementation, an image of dynamic optical properties of scattering medium such as, but not limited to, the vasculature of the human body in a cross-sectional view is provided. The technology employs low cost, compact instrumentation that uses non-damaging near infrared optical sources and features several alternate imaging heads to permit investigation of a broad range of anatomical sites.

In another implementation, the principles of the present invention can be used in conjunction with contrast agents such as absorbing and fluorescent agents. In another variant, the present invention allows the cross-sectional measurements of changes in

motion protocols such as in a start-stop fashion where the motor stops at a desired location thereby allowing the stable coupling of light into a transmitting fiber bundle. After the measurement at this source location is performed, the motor moves on to the next transmitting fiber. Motion control is in two-way communication with the timing control **104** thereby allowing precise timing of this procedure. Motion control allows the assignment of relative and/or absolute mirror positions allowing for precise alignment of the mirror with respect to the physical location of the fiber bundle. The mirror **306** is surrounded by a cylindrical shroud **309** in order to shield off stray light to prevent cross-talk. The shroud comprises an aperture **310** through which the light beam **302** passes toward the transmitting fiber. It is recognized and incorporated herein other schemes which may be used,(e.g., use of a fiber-optic switching device) to sequentially couple light into the transmitting fibers.

In an equivalent embodiment, fast switching of source positions is accomplished by using a number of light sources, each coupled into one of the transmitting fibers **306** which can be turned on and of each independently by electronic means.

The device employs the servo-motor control system **308** in FIG. 3 with beam steering optics, described above, to sequentially direct optical energy emerging from the source optics onto 1 mm diameter optical fiber bundles **306**, which are mounted in a circular array in the multiplexing input coupler **300**. The transmitting optical fiber bundles **306**, which are typically 2-3 meters in length are arranged in the form of an umbilical and terminate in the imaging head **206**.

Depending on the implementation, the apparatus of the present invention required for time-series imaging, employs the value of using a geometrically adaptive measurement head or imaging head. The imaging head of the present invention provides features that include, but are not limited to, 1) accommodating different size targets (e.g., breast); 2) stabilizing the target against motion artifacts; 3) conforming the target to well-defined geometry; and 4) to provide exact knowledge of locations for sources and detectors. Stability and a known geometry both contribute to the use of efficient numerical analysis schemes.

There are several different embodiments of the imaging head for data collection that may utilize the principles of the present invention. For example the use of an iris imaging head previously disclosed in the '322 and '355 patents , which are incorporated by reference in this disclosure, may be used with the principles of the present invention.

Described below are two exemplary imaging heads with the understanding that the invention may or may not use any type of imaging head, and if an imaging head is used, it would provide the features previously described.

As illustrated in FIG. 4, the iris unit can be employed as a parallel array of irises **402, 404, 406** enabling volume imaging studies. FIG. 4 illustrates how this can be configured for studying a medium **410**, in this example a human breast, using an imaging head **408**. As described previously, the medium used in the present invention can be any medium, which allows scattering of energy.

In one implementation of the imaging head illustrated in FIG. 5, is a flexible pad configuration. This planar imaging unit functions as a deformable array and is well suited to investigate body structures too large to permit transmission measurements (e.g.,

mm in diameter. Depending on the implementation, eighteen (18) of the sixty-three (63) fiber bundles may be arranged in an array to serve as both optical energy sources or energy transmitters, and receivers to sequentially deliver light to a designated target and receive emerging optical energy. In this implementation, the remaining forty-five (45) fiber bundles act only as receivers of the emerging optical energy.

The geometry of the illumination array is not arbitrary. The design shown in Figure 6 as an exemplary illustration has been configured, as have other implementations, to minimize the subsequent numerical effort required for data analysis while maximizing the source-density covered by the array. The fiber bundles are arranged in an alternating pattern as described by FIG. 6 and shown here with the symbols "X" and "0". In one implementation, a pattern of 00X000X00, X000X000X can be used on the imaging head. 'X' denotes a source/receiver fiber bundle, and '0' is a receiver only a receiver or detector fiber bundle. Basically, the design allows for the independent solution of two dimensional (2-D) image recovery problems from an eighteen (18) point source measurement. As a result, a composite three dimensional (3-D) image can be computed from superposition of the array of 2-D images oriented perpendicular to the target surface. Another advantage of this geometry is that it readily permits the use of parallel computational strategies without having to consider the entire volume under examination.

The advantage of this geometry is that each reconstruction data set is derived from a single linear array of source-detector fibers, thereby enabling solution of a 2-D problem without imposing undue physical approximations. The number of source-detector fibers belonging to an array can be varied. Scan speeds attainable with the 2-D array illustrated in FIG 6 are the same as for other imaging heads with 2-D arrays since

the scan speed depends only on the properties of the input coupler. Thus, faster scan speed are available for the creation of a 3-D image.

In another implementation, illustrated in FIG. 7, is an imaging head based on a "Hoberman" sphere geometry. In a Hoberman structure, the geometry is based on the intersection of a cube and an octahedron, which makes a folding polyhedron called a trapezoidal icosatetrahedron. This structure has been modified and implemented in a form of an imaging head of a hemispherical geometry. For many purposes of the instant invention, it is appropriate to use design features of smoothly varying surfaces based on the Hoberman concept of expanding structures. Depending on the implementation, other polygonal or spherical-type shapes may also be used with the principles of the present invention for other imaging head designs. Adjustment of the device in Figure 7 causes uniform expansion or contraction, thereby always preserving a hemispherical geometry. Imaging head **700** illustrates one example of modification to the "Hoberman" geometry. A receptacle for the fiber bundles **701** is disposed about imaging head **700**. Target volume **702** is where the medium would enter the imaging head in this implementation. This geometry is well suited for the investigation of certain tissues such as the female breast or the head. Depending on the implementation, attachment of optical fibers to the vertices of the hemisphere allows for up a seventeen (17) source by seventeen (17) detector measurement. The detectors or energy receivers may be disposed about the spherical imaging head and the detectors are located on the inner aspect of the expanding imaging head. Additional fiber bundles can be attached to the interlocking joints, permitting up to a 49 source by 49 detector measurement.

Depending on the implementation, light collected from the target medium is measured by using any of a number of optical detection schemes. One embodiment uses a fiber-taper, which is bonded to a charged coupled detector (CCD) array. The front end of the fiber taper serves to receive light exiting from the collection fibers. These fibers are preferably optical fibers, but can be any means that allows the transmission and reception of signals. The back end of the fiber taper is bonded to a 2-D charge-coupled-detector (CCD) array. In practice, use of this approach generally will require an additional signal attenuation module.

An alternate detection scheme employs an array of discrete photo detectors, one for each fiber bundle. This unit can be operated in a phase lock mode thereby allowing for improved rejection of ambient light signals and the discrimination of multiple simultaneously operated energy sources.

In another embodiment, in order to fulfill the demands posed by the desired physiological studies on the instrument, the following features characterize the detector system: scalable multi-channel design (up to 32 detector channels per unit); high detection sensitivity (below 10 pW); large dynamic range ($1{:}10^6$ minimum); multi-wavelength operation; ambient light immunity; and fast data acquisition (order of 100 Hz all-channel simultaneous capture rate).

To achieve this, the detector system uses photodiodes and a signal recovering technique involving electronic gain switching and phase sensitive detection (lock-in amplification) for each detector fiber (in the following referred to as detection or detector channels) to ensure a large dynamic range at the desired data acquisition rate. The phase sensitive signal recovery scheme not only suppresses electronic noise to a desired level

but also eliminates disturbances given by background light and allows simultaneous use of more than one energy source. Separation of signals from simultaneously operating sources can be achieved, as long as the different signals are encoded in sufficiently separated modulation frequencies. Since noise reduction techniques are based on the reduction of detection bandwidth, the system is designed to maintain the desired rate of measurements. In order to achieve a timing scheme that allows simultaneous readout of the channels, a sample-and-hold circuit (S/H) is used for each detection channel output. The analog signals provided by the detector channels are sampled, digitized and stored using the data acquisition system **116**. One aspect is the flexibility and scalability of the detection instrument. Not only are the detector channels organized in single, identical modules, but also the phase detection stages, each containing two lock-in amplifiers, are added as cards. In this way, an existing setup can easily be upgraded in either the number of detector channels and/or the number of wavelengths used (up to four) by cloning parts of the existing hardware.

FIG. 8 shows the block diagram of one implementation of a detector channel. In this implementation , two energy sources are being used. After detecting the light at the optical input **801** by a photo detector **802** the signal is fed to a transimpedance amplifier **803**. The transimpedance value of **803** is externally settable by means of digital signals **813** (PTA=Programmable Transimpedance Amplifier). This allows the adaptation to various signal levels thereby increasing the dynamic range of the detector channel. The signal is subsequently amplified by a Programmable Gain Amplifier (PGA) whose gain can be set externally by means of digital signals **814**. This allows for additional gain for

the lowest signal levels (e.g., in one implementation ~pW-nW) thereby thereby increasing the dynamic range of the detector channel.

In one embodiment, at least one energy source is used and the signal is sent to at least one of lock-in amplifiers (LIA) **805, 809**. Each lock-in amplifier comprises an input **808,812** for the reference signal generated by phase shifter **204** from FIG 2. After lock-in detection, the demodulated signal is appropriately boosted in gain by means of a programmable gain amplifier (PGA) **806, 810** in order to maximize noise immunity during further signal transmission and to improve digital resolution when being digitized. The gain of PGA **806, 810** is set by digital signals **815**.

At each output, a sample-and-hold circuit (S/H) **807, 811** is used for freezing the signal under digital timing by means of signal **816** for purposes described herein.

In one embodiment, the signal **815** is sent to **806, 810** in parallel. In one embodiment, the signal **816** is sent to **807, 811** in parallel.

As previously illustrated in FIG. 1, the analog signal provided by each of the channel outputs is sampled a data acquisition system **116**. In one embodiment, PC extension boards might be used for this purpose. PC extension boards also provide the digital outputs that control the timing of functions such as gain settings and sample-and-hold.

As previously noted, timing is crucial in order to provide the desired image capture rate and to avoid false readings due to detector-to-detector time skew. FIG. 9 shows one improvement of the invention over other timing schemes. With systems not comprising fast adaptable gain settings (such as some CCD based systems), a schedule according to **905** has to be implemented. The implementation in FIG 9 illustrates one use

of a silicon photo-diode in process **904**, which can be replaced by various detectors previously mentioned. A time series of data is acquired for a fixed source position. After finishing this task, the source is being moved **902** with respect to the target **901** and another series of data is being collected. Measurements are being performed in this fashion for all source positions. Every image **903** of the resulting time series of reconstructed images are being reconstructed from data sets merged together from the data for each source position. This schedule does not allow real-time capture of all physiologic processes in the medium and therefore only applies to certain modes of investigation. Although we are aware of the use of such schemes, e.g., when monitoring responses on repeatable maneuvers, the timing scheme for the invention very much improves on this situation.

Because the invention allows for fast source switching and large dynamic range and high data acquisition rates, a schedule indicated by **904** is performed. Here, the source position is switched fast compared to the dynamic features of interest and instantaneous multi-channel detection is performed at each source position. Images **903** are then reconstructed from data sets, which represent an instant state of the dynamic properties of the medium. Only one time series of full data sets (i.e., all source positions and all detector positions) is being recorded. Real time measurement of fast dynamics (e.g., faster 1 Hz) of the medium is provided by the invention.

FIG 10 shows one embodiment of a detailed schedule and sequence of the system tasks **1001** involved in collecting data at a source position and the proceeding of this process in time **1002**. Task **1003** is the setting of the optical de-multiplexer to a destined source position and setting the detectors to the appropriate gain settings. The source

position is illuminated for a period of time **1004**, during which the lock-in amplifiers settle **1005**. After the time it takes the S/H to sample the signal **1006**, the signal is being hold for a period of time **1007**, during which all channels are being read pout by the data acquisition. It is worthwhile noticing that during reading out the S/H, other tasks, like moving the optical source, setting the detector gains for the new source position, and settling of the lock-in, are being scheduled. This increases greatly the achievable data acquisition rate of the instrument.

This concept of a modular system is further illustrated in FIG. 11. Up to thirty-two (32) detector modules **1100** (each with 2 lock-in modules each for two modulation frequencies) are arranged using an enclosure **1102**. The cabinet also can carry up to two phase shifting modules **1104**, **1106**, each containing two digital phase shifter under computer control. The ability to adjust the reference phase with respect to the signal becomes necessary since unavoidable phase shifts in the signal may lead to non-optimum lock-in detection or can even result in a vanishing output signal. Organization of data, power supply and signal lines is provided by means of two back planes **1108, 1110**

Depending on the implementation, the detector system design illustrated in FIG. 8 allows one cabinet to operate at a capacity of 32 detectors with four different sources requiring 128 analog to digital circuit (ADC)-board input channels. The upper **1108** and the lower **1110** back plane are of identical layout and have to be linked in order to provide the appropriate distribution of supply-, control- and signal voltages. This is achieved using a 6U-module fitting both planes from the backside, that provides the necessary electric linking paths, and interfaces for control- and signal lines.

FIG. 12 shows the schematic of one implementation of a channel module. In this implementation, a silicon photodiode 1206 is used as the photo-detector. A Programmable Transimpedance Amplifier (PTA) **1201** is formed by an operational amplifier **1204** , resistors **1201** and **1202** and an electronic switch **1205**, the latter of which is realized using a miniature relay. Other forms of electronic switches such as analog switches might be used. Relay **1205** is used to connect or disconnect 1203 from the circuit thereby changing the transimpedance value of **1201**. A high-pass filter (R2, C5) is used to AC-couple the subsequent programmable gain instrumentation amplifier **IC2** (Burr Brown PGA202) in order to remove DC offset. The board-to-board connectors for the two lock-in-modules are labeled as "slot A" **1210** and "slot B" **1212**. The main connector to the backplane is a 96-pole DIN plug **1220**.

FIG. 13, illustrates the electric circuit of the lock in modules **1210**, **1212**. The signal is subdivided and passed to two identical lock-in-amplifiers, each of which gets one particular reference signal according to the sources used in the experiment. The signal is first buffered **IC1, IC7** (AD LF111) and then demodulated using an AD630 double-balanced mixer **IC2, IC8**.

In order to remove undesired AC components, the demodulated signal passes through an active 4-pole Bessel-type filter **IC3, IC4, IC 9, IC10** (Burr Brown UAF42). A Bessel-type filter has been chosen in order to provide fastest settling of the lock-in amplifier for a given bandwidth. Since a Bessel-filter shows only slow stopband-transition, a 4-pole filter is being used to guarantee sufficient suppression of cross talk between signals generated by different sources (i.e. of different modulation frequency). The filter has its 3 dB point at 140 Hz, resulting in 6 ms settling time for a step response

(<1% deviation of actual value). The isolation of frequencies separated by 1 kHz is 54 dB. The filters are followed by a programmable gain amplifier **IC5, IC 11**, whose general function has been described above. The last stage is formed by a sample-and-hold chip (S/H) **IC6, IC12** (National LF398).

In another implementation, the phase sensitive detection can be achieved with digital methods using digital signal processing (DSP) components and algorithms. The advantage of using DSP with the principles of the present invention is improved lectronic performance and enhanced system flexibility.

In another implementation, an analog-to-digital converter is used for each detector channel thereby improving noise immunity of the signals.

Although illustrative embodiments have been described herein in detail, those skilled in the art will appreciate that variations may be made without departing from the spirit and scope of this invention. Moreover, unless otherwise specifically stated, the terms and expressions used herein are terms of description and not terms of limitation, and are not intended to exclude any equivalents of the system and methods set forth in the following claims.

What is claimed is:

1. A system for use in tomographic imaging of a scattering medium, comprising:

an energy source for emitting a signal and having at least one energy transmitter coupled thereto; and

a detection system coupled to the energy source and including at least one energy receiver for measuring dynamic properties of the scattering medium.

2. The system of claim 1, further including an imaging head coupled as the energy transmitter and energy receiver for holding thereof.

3. The system of claim 1, wherein the detection system further comprises at least one lock-in amplifier for separating a signal emitted by at least one energy source.

4. The system of claim 1, wherein the detection system further includes at least one gain adjustment means for increasing dynamic range of the detector system.

5. The system of claim 1, wherein the detection system further includes a sample-and-hold circuit for freezing the signal emitted by the energy source.

6. The system of claim 5, wherein the sample-and-hold circuit further includes logic for allowing simultaneous readout for each detector fiber.

7. The system of clam 1, wherein the energy source includes at lest one of non-laser optical sources, LED and high-pressure incandescent lamp, laser diodes, solid state lasers, titanium-sapphire laser, ruby laser, dye laser, electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and combinations thereof.

8. The system of claim 1, wherein data acquisition from the detection system is about 150Hz.

9. The system of claim 1, wherein the energy source includes a plurality of near infra red laser diodes to transmit multiple wavelengths.

10. A detection system to collect data about the dynamic properties of a scattering medium, comprising:

at least one energy receiver for detecting a signal from an energy source; and

a programmable gain instrumentation amplifier for increasing the dynamic range of the signal which provides rapid data acquisition about the dynamic properties of the scattering medium.

11. The detection system of claim 10, wherein the energy receiver includes at least one of a photo-diode, PIN diode, Avalanche photodiodes , change couple device, change inductive device, photo-multiplier tubes, multi-channel plate, acoustic transducers, and any combinations thereof.

12. The detection system of claim 10, further including a sample-and-hold circuit coupled to the programmable gain instrumentation amplifier that allows simultaneous readout of a plurality of signals from the energy source.

13. A system for use in optical tomographic imaging of a scattering medium comprising:

at least one energy transmissive fiber bundle coupled to an energy source;

an imaging head for holding the energy transmissive fiber bundle; and

a detection system for collecting data about the optical dynamic properties of the scattering medium.

14. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

15. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

16. The system of claim 13, wherein the imaging head is a folding sphere or polygon.

17. The system of claim 16, wherein the polygon is a polyhedron or a trapezoidal icosatetrahedron, or a hemitrapezoidal icosatetrahedron..

18. The system of claim 16, wherein the fiber bundle is disposed about the imaging head.

19. The system of claim 13 wherein the fiber bundle has a diameter of about 3 mm.

20. The system of claim 13, wherein the imaging head further includes adjustment means for accommodating different size medium, stabilizing the medium against motion artifacts, conforming the target to a simple well-defined geometry and

providing information about the location of at lest the receiver in reference to the location of the transmitter.

21. A method of using optical tomographic imaging, comprising:

(a) exposing a scattering medium to near infra-red light; for collecting data about the dynamic properties of a scattering medium,

(b) detecting light by a detection system; and

(c) enhancing gain through a programmable gain instrumentation amplifier for the purpose of measuring the dynamic properties of the scattering medium.

22. The method of claim, wherein the scattering medium is vascular tissues.

23. The method of claim 21, further including separating via at least one lock-in amplifier a plurality of wavelengths transmitted through the medium.

24. The method of claim 21, further including collecting data from simultaneous readouts of a signal.

25. A system for optical tomographic imaging of a medium comprising:

an imaging head having at least one source disposed to direct optical energy into a medium and a plurality of detectors disposed to receive optical energy emerging from the medium, the detectors means being located at a plurality of distances from the source constituting a plurality of distances through the medium the detectors and thee source , the source and detectors forming respective source detector pairs;

a programmable gain amplifier connected to amplify at least one signal of the source detector pairs;

a computer having a data acquisition board for receiving the signal from the programmable gain amplifier and reconstructing an image of the medium.

26. The system of claim 25, wherein the optical energy comprises optical energy of at least two different intensity modulated wavelengths of energy.

27. The system of claim 26, further comprising a filtering means for separating signals corresponding to a wavelength of intensity modulated energy.

28. The system of claim 25, further comprising a sample and hold circuit for holding a desired signal for use in measuring of dynamic properties of the medium.

29. The system of claim 25, wherein the source comprises energy transmissive fibers coupled to an energy emitting source.

30. The system of claim 25, wherein the source comprises a plurality of optical energy sources.

31. The system of claim 25, wherein the source comprises of plurality of laser diodes.

32. The system of claim 25, wherein the detectors are fibers coupled to optical energy detectors.

33. The system of claim 25, wherein the detectors are optical energy detectors.

34. An imaging head comprising

a pad;

a plurality of source means for delivering optical energy to a medium; and

a plurality of detector means for detecting optical energy emerging from a medium, the source means and detector means being attached to the pad in a plurality of rows and columns wherein the plurality of source means are arranged to form at least two unique imaging planes, an imaging plane being between defined by a plane substantially perpendicular to the pad and passing through at least two source means and one detector means.

35. The imaging head of claim 34, wherein a plurality of source means and detector means are joined to form combined source detector means, the combined source detector means and detector means being arranged in an alternating rows of a first pattern and a second pattern, the first pattern comprising one combined source detector means followed by three detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means, the second pattern comprising two detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means followed by two detector means.

36. The imaging head of claim 34, wherein the source means are fibers coupled to an optical energy source.

37. The imaging head of claim 34, wherein the source means are optical energy sources.

38. The imaging head of claim 34, wherein the source means is laser diodes.

39. The imaging head of claim 34, wherein the detector means are fibers coupled to optical energy detectors.

40. The imaging head of claim 34 wherein the detector means are optical energy detectors.

41. The imaging head of claim 34 wherein the detector means are photodiodes.

42. An adjustable imaging head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements, each trust element having a central pivot point, an internal terminal pivot point and an external terminal pivot point that do not lie on a straight line, each strut being pivotally joined to the other of its pair by their central pivot points, each strut being pivotally joined by the internal terminal pivot point and the external terminal pivot point to the internal terminal pivot point and the external terminal pivot point respectively of another scissors pair, whereby an adjustable ring of principle vertices is formed by the internal terminal pivot points and whereby adjustment causes uniform movement of the principle vertices, the improvement comprising:

at least one source means for delivering optical energy into a medium and at least one detector means for detecting optical energy emerging from a medium, wherein the source means and the detector means are attached to the principle vertices, the source means being oriented to direct optical energy substantially toward a medium in

the center of the ring, the detector means being oriented to receive optical energy emerging substantially from a medium in the center of the ring.

43. The adjustable imaging head of claim 42, further comprising:

amount in communication with a truss element, wherein the mount supports the imaging head and regulates the size of the adjustable ring.

44. The adjustable imaging head of claim 42, further comprising:

a first set of mounts in communication with a first set of diametrically opposed external terminal pivot points;

a second set of mounts in communication with a second set of diametrically opposed external terminal pivot points, wherein the first set of diametrically opposed external terminal pivot points is orthogonal to the second set of diametrically opposed external terminal pivot points,

a drive system in communication with at least one of the mounts in at least one of the first or second sets of mounts, whereby the drive system regulates the size of the adjustable ring.

45. The imaging head of claim 42, wherein the source means are fibers coupled to an optical energy source.

46. The imaging head of claim 42, wherein the source means are optical energy sources.

47. The imaging head of claim 42, wherein the source means are laser diodes.

48. The imaging head of claim 42, wherein the detector means are fibers coupled to optical energy detectors.

49. The imaging head of claim 42, wherein the detector means are optical energy detectors.

50. The imaging head of claim 42, wherein the detector means are photodiodes.

51. An imaging head for use in optical tomography, comprising:

at least one energy receiver;

adjustment means for accommodating different sizes of the medium; and

communication means for transmitting signals from the imaging head to a detection system for use in the measurement of dynamic properties of a scattering medium.

52. The imaging head of claim 49, further including at least one energy transmitter.

53. The imaging head of claim 52, wherein the energy transmitters define an illumination array configured to minimize subsequent numerical effort required for data analysis and maximizing source density covered by the array.

54. The imaging head of claim 53, wherein three dimensional images can be computed from super positioning of the array of two dimensional images.

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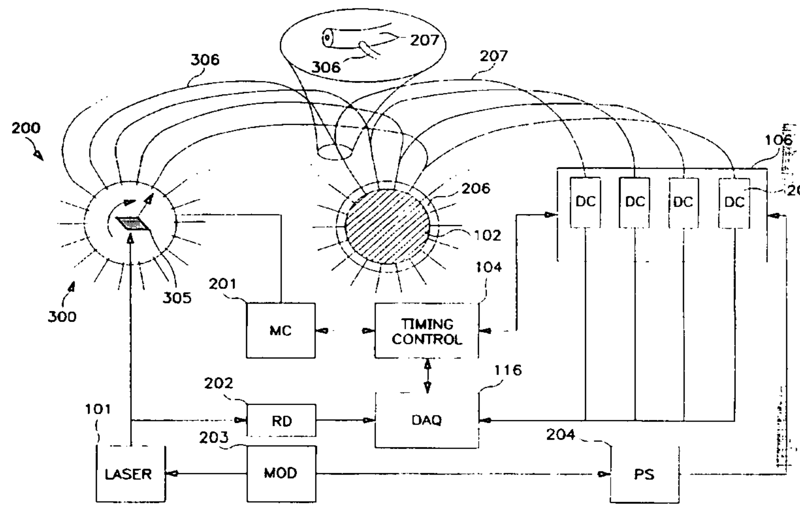
(54) Title: SYSTEM AND METHOD FOR TOMOGRAPHIC IMAGING OF DYNAMIC PROPERTIES OF A SCATTERING MEDIUM



(57) Abstract: A system and method for the detection and three dimensional imaging of absorption and scattering properties of a medium such as human tissue is described. According to one embodiment of the invention, the system directs optical energy toward a turbid medium from at least one source and detects optical energy emerging from the turbid medium at a plurality of locations uisng at least one detector (106). The optical energy emerging from the medium (102) and entering the detector (106) originates from the source (101) is scattered by the medium (102). The system then generates an image representing interior structure of the turbid medium based on the detected optical energy emerging from the medium (102). Generating the image includes a time-series analysis.

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SYSTEM AND METHOD FOR TOMOGRAPHIC IMAGING OF DYNAMIC PROPERTIES OF A SCATTERING MEDIUM

This invention was made with U.S. Government support under contract number CA-RO166184-02A, awarded by the National Cancer Institute. The U.S. Government has certain rights in the invention.

This application claims the benefit under 35 U.S.C. §120 of prior U.S. Provisional Patent Application Serial Nos. 60/153,926 filed September 14, 1999, entitled DYNAMIC TOMOGRAPHY IN A SCATTERING MEDIUM and 60/154,099 filed September 15, 1999, entitled DYNAMIC TOMOGRAPHY IN A SCATTERING MEDIUM.

This application is related to copending application serial number "not yet assigned", attorney docket number 0887-4147PC2, filed on the same date as this application, entitled "METHOD AND SYSTEM FOR IMAGING THE DYNAMICS OF SCATTERING MEDIUM" by inventor R. Barbour is hereby incorporated by reference (hereinafter the "Barbour 4147PC2 application").

This application is also related to copending application serial number "not yet assigned", attorney docket number 0887-4149PC1, filed on the same date as this application, entitled "METHOD AND SYSTEM FOR ENHANCED IMAGING OF A SCATTERING MEDIUM" by inventors R. Barbour and Y Pei and is hereby incorporated by reference (hereinafter the "Barbour 4149PC1 application").

This application is also related to copending application serial number "not yet assigned", attorney docket number 0887-4149PC2, filed on the same date as this application, entitled "IMAGING OF SCATTERING MEDIA USING RELATIVE DETECTOR VALUES" by inventor R. Barbour and is hereby incorporated by reference (hereinafter the "Barbour 4149PC2 application").

Field of the Invention

The invention relates to a system and method for tomographic imaging of dynamic properties in of a scattering medium, which may have special application to medical imaging, and in particular to systems and methods for tomographic imaging using near infrared energy to image time variations in the optical properties of tissue.

Background of the Invention

Contrary to imaging methods relying on the use of ionizing radiation and/or toxic/radioactive contrast agents, near infra-red (NIR)-imaging methods bear no known risk of causing harm to the patient. The dose of optical intensity used remains far below the threshold of thermal damage and is therefore safe. In the regime of wavelength/ intensity/power used, there are no effects on patient tissue that accumulate with increasing NIR dose due to over-all irradiation time.

The general technology involved in optical tomography is developed and understood, so that, compared to other cross-sectional imaging techniques such as MRI, X-ray CT, and the like, only moderate costs and relatively small-sized devices are required. Optical tomography especially gains from the development of small, economical, yet powerful semiconductor lasers (laser diodes) and the availability of highly integrated, economical off-the-shelf data processing electronics suitable for the application. Moreover, the availability of powerful yet inexpensive computers contributes to the attractiveness of optical tomography since a significant computational effort may be necessary for both image reconstruction and data analysis.

Optical tomography yields insights into anatomy and physiology that are unavailable from other imaging methods, since the underlying biochemical activities of

physiological processes almost always leads to changes in tissue optical properties. For example, imaging blood content and oxygenation is of interest. Blood shows prominent absorption spectra in the NIR region and vascular dynamics and blood oxygenation play a major role in physiology/pathology.

However, cross-sectional or volumetric imaging of dynamic features in large tissue structures is not extractable with current optical imaging methods. At present, whereas a variety of methods involving imaging and non–imaging modalities are available for assessing specific features of the vasculature, none of these assess measure dynamic properties based on measures of hemoglobin states. For instance, detailed images of the vascular architecture involving larger vessels (> 1 mm dia.) can be provided using x–ray enhanced contrast imaging or MR angiography. These methods however are insensitive to hemoglobin states and only indirectly provide measures of altered blood flow. The latter is well accomplished, in the case of larger vessels, using Doppler ultrasound, and for near–surface microvessels by laser Doppler measurements, but each is insensitive to variations in tissue blood volume or blood oxygenation. Ultrasound measurements are also limited by their ability to penetrate bone. Other methods are available, (*e.g.*, pulse volume recording, magnetic resonance (MR) BOLD method, radioscintigraphic methods), and each is able to sample, either directly or indirectly, only a portion of the indicated desired measures.

Thus, there is a need for a system and method of data collection providing cross-sectional or volumetric imaging of dynamic features in large tissue structures.

SUMMARY OF THE INVENTION

The present invention provides a system and method for generating an image of dynamic properties in a scattering medium. The system includes an energy source, such as a NIR emitting source, and a detection system to measure received energy. In an exemplary embodiment, the detection system has at least one photo-detector such as a photodiode, a means for rapid adjustment of signal gain, and a device for retaining a measured response in order to investigate the dynamic variations in the optical properties of tissues. Depending on the implementation, the detection system further may also include at least one means for separating a plurality of signals from the photo-receiver when multiple energy sources are used simultaneously. This simultaneous use of multiple energy sources allows the use of different wavelengths and/or different source locations at the same time.

In one implementation using optical tomographic imaging, a specimen is exposed to NIR light emitted from at least one laser diode. Furthermore an imaging head may be utilized that contains means for positioning at least one source location and / or at least one detector location with respect to the medium. The energy detector may use an energy collecting element, such as an optical fiber to transmit the received energy. The energy detector is responsive to the energy or light emerging from the specimen. In accordance with the invention, the signal from the detector is selectively enhanced in gain to increase the dynamic measurement range. The method may further include separating via at least one lock-in amplifier a plurality of signals generated by multiple energy sources. In addition, the method allows simultaneous measurements of signals produced by the NIR light by means of a sample-and-hold circuit when more than one detector fiber is used.

BRIEF DESCRIPTION OF THE FIGURES

For a better understanding of the invention, together with the various features and advantages thereof, reference should be made to the following detailed description of the preferred embodiments and to the accompanying drawings wherein:

FIG. 1 is a block diagram of one embodiment of a system according to the invention;

FIG. 2 is a block diagram illustrating one implementation of the system in FIG. 1;

FIG. 3 is a perspective view of a servo-motor apparatus useful in this invention to illuminate a number of fiber bundles with a single energy source;

FIG. 4 is a schematic illustration of the disposition for examining human tissue such as a human breast;

FIG. 5 is a photograph of a planar imaging head useful in one embodiment of the invention;

FIG. 6 is one embodiment for the source detector arrangement on the imaging head shown in FIG. 5;

FIG. 7 is an illustration of a spherical imaging head useful in practicing the invention;

FIG. 8 is a block diagram of a detector channel useful in practicing the invention;

FIG. 9 is a graphical representation of one implementation of a timing scheme used in the system of FIG.1;

FIG. 10 is a diagram illustrating the sequence of certain events in a multiple channel embodiment of the invention;

FIG. 11 is a schematic illustration of the physical arrangement of multiple detector channels used in a preferred embodiment of the invention;

FIG. 12 is a circuit diagram of one detector channel used in FIG. 11; and

FIG. 13 is a circuit diagram of one implementation of the lock-in module used in FIG 12.

DETAILED DESCRIPTION OF THE INVENTION

The objective of the invention is to provide a system and method capable to extract dynamics in properties of a scattering medium. The use of the invention's system and method has several applications including, but not limited to, medical imaging applications. Although the methods described herein focus on tomographic imaging the dynamic properties of hemoglobin states and tissue using optical tomography, with an imaging source generating multiple wavelengths in the NIR region, it is appreciated that the invention is applicable to any medium that is able to scatter the propagating energy from any energy source, including external energy sources such as those sources located outside the medium and/or internal sources such as those energy sources located inside the medium. For example, other media includes, but are not limited to, medium from mammals, botanical life, aquatic life, or invertebrates; oceans or water masses; foggy or gaseous atmospheres; earth strata; industrial materials; man-made or naturally occurring chemicals and the like. Energy sources include, but are not limited to, non-laser optical sources like LED and high-pressure incandescent lamps and lasers sources such as laser diodes, solid state lasers such as titanium-sapphire laser and ruby laser, dye laser and

other electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and any combinations thereof.

Similarly the means to detect the signal produced by the energy source is not limited to photodiode implementation discussed in one of the preferred embodiments further described herein. Other detectors can be used with the principles of the present invention for the purpose of tomographic imaging the dynamic properties of a medium. Such detectors include for example, but are not limited to, photo-diodes, PIN diodes (PIN), Avalanche Photodiodes (APD), charge couple device (CCD), charge inductive device (CID), photo-multiplier tubes (PMT), multi-channel plate (MCP),acoustic transducers and the like.

The present invention builds upon previous disclosures in U.S. Patent Nos. 5,137, 355 ("the '355 patent") entitled "Method of Imaging a Random Medium" ("the '355 patent") and 6,081,322 ("the '322 patent") entitled "NIR Clinical Opti-Scan System", the disclosures of both the '355 and '322 patents are incorporated herein by reference. Disclosed in these patents is an approach to optical tomography, and the instrumentation required to accomplish the tomography. The modifications in the present invention provide fast data acquisition, and new imaging head designs. Fast data acquisition allows accurate sampling of dynamic features. The modification in the imaging head allows accommodation of different size targets (e.g., breast); the stabilization of the target against motion artifacts; conforming the target to a simple well-defined geometry; and knowledge of source and detector positioning on or about the target. All of the enumerated features listed above for the imaging head is crucial for accurate image reconstruction.

Additionally, the present invention uses detector circuitry that allows quick adaptation of the measurement range to the signal strength thereby increasing the over-all dynamic range. "Dynamic range" for the purposes of this description means the ratio between the highest and lowest detectable signal. This makes the circuitry suitable for use with source-detector distances that can vary significantly during the data collection, thereby allowing fast data acquisition over wide viewing angles. For instance, we are aware that dynamic features of dense scattering media may be extractable from measurements using a single source and single detector at a fixed distance between each other. Depending on the implementation, such an arrangement could be made using a detector of relatively small dynamic range. Although we are aware of the possible usefulness of such a measurement, our invention allows the measurement of dynamics in optical properties of dense scattering media using source-detector pairs over a wide range of distances (e.g., greater than or about 5 cm). Such full tomographic measurements allow for improved accuracy in image reconstruction.

Depending upon the implementation, it is within the scope of the present invention to include those embodiments using a restricted source detector distance and therefore not requiring fast gain adjustment. For example, in one embodiment, the system of the present invention can also be operated using detector channels of low-dynamic range (e.g., 1:1000) when detector fibers of a fixed distance from the source are being used for the measurement (e.g., the detector opposite the source).

The data collection scheme of the present invention disclosed herein provides time-series of raw data sets that provide useful information about dynamic properties of the scattering medium without any further image reconstruction. For example, by

displaying the raw data in a color mapping format, features can be extracted by sole visual inspection. In addition to that, analysis algorithms of various types such as, but not limited to, linear and non-linear time-series analysis or pattern recognition methods can be applied to the series of raw data. The advantage of using these analytical methods is the improved capability to reveal dynamic signatures in the signals.

In another implementation, image reconstruction methods may be applied to the sets of raw data thereby providing time series of cross-sectional images of the scattering medium. For these implementations, analysis methods of various types such as, but not limited to, linear and non-linear time-series analysis, filtering, or pattern recognition methods can be applied. The advantage of using such analysis is the improved extraction of dynamic features and cross-sectional view, thereby increasing diagnostic sensitivity and specificity. These methods are explained in detail in the '355 and '322 patents, which were previously described and incorporated in as reference.

The invention reveals measurements of real-time spatial temporal dynamics. Depending on the implementation, an image of dynamic optical properties of scattering medium such as, but not limited to, the vasculature of the human body in a cross-sectional view is provided. The technology employs low cost, compact instrumentation that uses non-damaging near infrared optical sources and features several alternate imaging heads to permit investigation of a broad range of anatomical sites.

In another implementation, the principles of the present invention can be used in conjunction with contrast agents such as absorbing and fluorescent agents. In another variant, the present invention allows the cross-sectional measurements of changes in

optical properties due to variations in temperature. The advantage of this variant is seen, but not restricted to, the use of monitoring cryosurgery.

A system using the modified instrumentation and described methods of the instant invention is capable of producing cross-sectional images of real-time events associated with vascular reactivity in a variety of tissue structures (e.g., limbs, breast, head and neck). Such measurements permit an in-depth analysis of local hemodynamic states that can be influenced by a variety of physiological manipulations, pharmacological agents or pathological conditions. Measurable physiological parameters include identification of local dynamic variations in tissue blood volume, blood oxygenation, estimates of flow rates, and tissue oxygen consumption. It is specifically noted that measurements of several locations on the same medium can be taken. For example, measurements may be taken of the leg and arm areas of a patient at the same time. Correlation of data between the different locations is available using the methods described herein.

The invention also provides both linear and non-linear time series analysis to reveal site specific functionality of the various components of the vascular tree. Thus the response characteristics of the major veins, arteries and structures associated with the microcirculation can be evaluated in response to a range of stimuli.

Fast data collection methods are particularly helpful because there are many disease states with specific influences on the spatial-dynamic properties of vascular responses. Accordingly, it is understood that significantly greater contrast mechanisms are definable, with much greater diagnostic sensitivity. This is accomplished by collecting and evaluating data in the time domain. These results are not available by performing static imaging studies.

The importance of dynamic properties follows directly from an understanding of the well known physiological reactivity of the vascular system. Control of the peripheral vasculature is mediated by neural, humoral and metabolic factors. Neural control is principally through autonomic activity. The details of these properties are well known to many, and can be found in any one of several medical physiology texts. Loss of autonomic control occurs in a variety of disease processes, especially in diabetes. Invariably, this loss of control will adversely influence local perfusion states. The current invention has the capacity to directly evaluate the concept known as vascular sufficiency. This term takes into account the fact that, among its many roles, the vasculature is uniquely responsible for the delivery of essential nutrients to tissue, in particular, oxygen, and for the removal of metabolic waste products. Imbalances between supply and demand lead to relative hypoxic states, which often are clinically significant.

FIG. 1 illustrates one embodiment of the invention. Shown is a system **100** comprising medium **102**. The medium can be any medium in which the propagation of the used source energy is strongly affected by scattering.

From a source module **101** energy is directed to the medium **102** from which the exiting energy is measured by means of detector **106**, further discussed below. As previously discussed, there is a variety of sources, media, and detectors that may be used with the principles of the present invention. The following is a discussion of a sampling of such elements with the intention to describe how the invention is realized. In no way are these examples meant, nor do they intend to limit the invention to these implementations. A variation of elements as described herein may also utilize the principles of the present invention.

In one implementation, measurements of dynamics in the optical properties of the medium is accomplished by using optical source energy and performing rapid detection of the acoustic energy created by absorption processes in the medium. This can be implemented using both pulsed and harmonic modulated light sources, the latter allowing for lock-in detection. Detectors can be, but are not limited to, piezo-electric transducers such as PZT crystals or PVDF foils.

In another variant, a timing and control facility **104** is used to coordinate source and detector operation. This coordination is further described below. A device **116** provides acquisition and storage of the data measured by the detector **106**. Depending on the implementation, control and timing of the system's components is provided by a computer, which includes a central processor unit (CPU), volatile and non-volatile memory, data input and output ports, data and program code storage on fixed and removable media and the like. Each main component is described in greater detail below.

FIG. 2 illustrates another implementation of a preferred embodiment of the present invention. Shown is a system and method that incorporates at least one wavelength measurement. Depending upon the implementation, this measurement is accomplished by alternately coupling light from diode lasers into transmitting fibers arranged in a circular geometry.

Referring again to FIG. 2, a system **200** includes an energy source, which in this implementation includes one or more laser **101**. A reference detector **202** is used to monitor the actual output power of laser **101** and is coupled to a data acquisition unit **116**. Such laser may be a laser diode in the NIR region. The laser is intensity modulated by a modulation means **203** for providing means of separation of background energy sources

such as daylight. The modulation signal is also send to a phase shifter **204** whose purpose is described further below. The light energy generated by the laser **101** is directed into an optical de-multiplexing device **300** further discussed in detail below. Using a rotating mirror **305**, the light is being directed into one of several optical source fiber bundles **306** that are used to deliver the optical energy to the medium **102**. To provide good optical contact and measurement fidelity, one of several possible imaging heads **206** as described further below is used. A motor controller **201** is coupled to the de-multiplexing device **300** for controlling the motion of the rotating mirror **305**. The motor controller **201** is also in communication with a timing control **104** for controlling the timing of the motion of mirror **305**.

The measuring head **206** comprises the common end of a bifurcated optical fiber bundle, whose split ends are formed by the source fiber bundle **306** and detector fiber bundle **207**. Source fiber bundle **306** and detector fiber bundle **207** form a bulls eye geometry at the common end with the source fiber bundle in the center. In other embodiments, source and detector bundles are arranged differently at the common end (e.g., reversed geometry or arbitrary arrangement of the bundle filaments). The common end of a bifurcated optical fiber bundle, preferably comes in contact with the medium, however, this embodiment is not limited to contact with the medium. For example, the common ends may simply be disposed about the medium. The signal is transmitted from the detector fiber bundle **207** to a detector unit **106** that comprises at least one detector channel **205** further described herein.. The detector channel **205** is coupled to the data acquisition unit **116** and the timing control unit **104**. Depending on the implementation, a phase shifter **204** may or may not be used, and is coupled to the detector unit **106** for the

purposes of providing a reference signal for the purposes of filtering the signal received from bundle **207**.

Depending on the implementation, illustrated in FIG. 3 is a device for the measurement of the dynamic properties of a scattering medium. This measurement is performed by sequentially reflecting light **302** off of a rotatable front surface mirror **306**, mounted at a 45 degree angle to the incident source, into source fibers **306** arranged in a circular geometry about the rotating optic. The rotation is done by a motor **308** with a shaft **307** to which the mirror is attached. This embodiment has an advantage of enabling fast switching among the transmitting fibers. In particular, it provides the ability to introduce beam shaping optics between the reflective mirror and transmitting fibers thereby allowing fine adjustment of the illumination area available for coupling into the fibers. This is useful because it allows independent adjustment of the rotation speed of the reflective optic (i.e., switching speed), and the illumination time allowed for each transmitting fiber bundle. Thus, a range of illumination frequencies can be employed while allowing fine adjustment of the illumination time at each source position to permit collection of data having a suitable signal-to-noise ratio.

Light from laser **101** is transmitted to unit **300** by means of transmitting optics **303** including, but not limited to, fiber optics and free propagating beams. Further beam shaping optics **301** may be used to optimize in -coupling efficiency into the transmitting fibers. Units **303** and **301** are under mechanical fine adjustment in their position with respect to the mirror **309**.

Motor **308** is operated under control of motion control **201** to allow for precise positioning and timing. By this means, it is possible to operate the motor under complex

motion protocols such as in a start-stop fashion where the motor stops at a desired location thereby allowing the stable coupling of light into a transmitting fiber bundle. After the measurement at this source location is performed, the motor moves on to the next transmitting fiber. Motion control is in two-way communication with the timing control **104** thereby allowing precise timing of this procedure. Motion control allows the assignment of relative and/or absolute mirror positions allowing for precise alignment of the mirror with respect to the physical location of the fiber bundle. The mirror **306** is surrounded by a cylindrical shroud **309** in order to shield off stray light to prevent cross-talk. The shroud comprises an aperture **310** through which the light beam **302** passes toward the transmitting fiber. It is recognized and incorporated herein other schemes which may be used,(e.g., use of a fiber-optic switching device) to sequentially couple light into the transmitting fibers.

In an equivalent embodiment, fast switching of source positions is accomplished by using a number of light sources, each coupled into one of the transmitting fibers **306** which can be turned on and of each independently by electronic means.

The device employs the servo-motor control system **308** in FIG. 3 with beam steering optics, described above, to sequentially direct optical energy emerging from the source optics onto 1 mm diameter optical fiber bundles **306**, which are mounted in a circular array in the multiplexing input coupler **300**. The transmitting optical fiber bundles **306**, which are typically 2-3 meters in length are arranged in the form of an umbilical and terminate in the imaging head **206**.

Depending on the implementation, the apparatus of the present invention required for time-series imaging, employs the value of using a geometrically adaptive measurement head or imaging head. The imaging head of the present invention provides features that include, but are not limited to, 1) accommodating different size targets (e.g., breast); 2) stabilizing the target against motion artifacts; 3) conforming the target to well-defined geometry; and 4) to provide exact knowledge of locations for sources and detectors. Stability and a known geometry both contribute to the use of efficient numerical analysis schemes.

There are several different embodiments of the imaging head for data collection that may utilize the principles of the present invention. For example the use of an iris imaging head previously disclosed in the '322 and '355 patents , which are incorporated by reference in this disclosure, may be used with the principles of the present invention.

Described below are two exemplary imaging heads with the understanding that the invention may or may not use any type of imaging head, and if an imaging head is used, it would provide the features previously described.

As illustrated in FIG. 4, the iris unit can be employed as a parallel array of irises **402, 404, 406** enabling volume imaging studies. FIG. 4 illustrates how this can be configured for studying a medium **410**, in this example a human breast, using an imaging head **408**. As described previously, the medium used in the present invention can be any medium, which allows scattering of energy.

In one implementation of the imaging head illustrated in FIG. 5, is a flexible pad configuration. This planar imaging unit functions as a deformable array and is well suited to investigate body structures too large to permit transmission measurements (e.g.,

head and neck, torso, and the like). Using this type of imaging head, optical measurements are made in a back-reflection mode. Optical fiber bundles **502** originating from the optical multiplexing input coupler **112** (described elsewhere) terminate at the deformable array or flexible pad **500**. The pad can be made of any flexible material such as black rubber or the like. The optical fiber bundles may be bifurcated and have ends **504** that both transmit and receive light. More than one pad may or may not be used, although an additional pad is not necessary for the purpose of the present invention, or for measurement application to other portions of the medium or to the same medium. For example, in the case of a breast exam, both pads maybe applied to the same breast having one pad above and one pad below the breast. In addition, one pad maybe applied to the right breast by having the pad deformed around the breast. Similarly, the other pad may be applied to the left breast. This configuration would allow both breasts to be examined at the same time. In addition, information may be correlation between the data collected from the two different members of the body. Again, the invention can be applied to other media and is not limited to portions of the human body. Thus, correlation between different media may be collected using this technique.

As further shown in Figure 5, the additional pad would have similar functions as the pad previously described and would have optical fiber bundles **503**, flexible pad **505**, and bifurcated optical fiber bundle ends **501** similar to the previous pad described. The array itself can be deformed to conform to the surface of a curved medium to be imaged (e.g. portion of the torso). The deformable array optical energy source and receiver design includes, depending on the implementation, a 7 x 9 array (63 total bundles) of optical fiber bundles as illustrated in FIG 6. In one variant, each bundle is typically 3

mm in diameter. Depending on the implementation, eighteen (18) of the sixty-three (63) fiber bundles may be arranged in an array to serve as both optical energy sources or energy transmitters, and receivers to sequentially deliver light to a designated target and receive emerging optical energy. In this implementation, the remaining forty-five (45) fiber bundles act only as receivers of the emerging optical energy.

The geometry of the illumination array is not arbitrary. The design shown in Figure 6 as an exemplary illustration has been configured, as have other implementations, to minimize the subsequent numerical effort required for data analysis while maximizing the source-density covered by the array. The fiber bundles are arranged in an alternating pattern as described by FIG. 6 and shown here with the symbols "X" and "0". In one implementation, a pattern of 00X000X00, X000X000X can be used on the imaging head. 'X' denotes a source/receiver fiber bundle, and '0' is a receiver only a receiver or detector fiber bundle. Basically, the design allows for the independent solution of two dimensional (2-D) image recovery problems from an eighteen (18) point source measurement. As a result, a composite three dimensional (3-D) image can be computed from superposition of the array of 2-D images oriented perpendicular to the target surface. Another advantage of this geometry is that it readily permits the use of parallel computational strategies without having to consider the entire volume under examination.

The advantage of this geometry is that each reconstruction data set is derived from a single linear array of source-detector fibers, thereby enabling solution of a 2-D problem without imposing undue physical approximations. The number of source-detector fibers belonging to an array can be varied. Scan speeds attainable with the 2-D array illustrated in FIG 6 are the same as for other imaging heads with 2-D arrays since

the scan speed depends only on the properties of the input coupler. Thus, faster scan speed are available for the creation of a 3-D image.

In another implementation, illustrated in FIG. 7, is an imaging head based on a "Hoberman" sphere geometry. In a Hoberman structure, the geometry is based on the intersection of a cube and an octahedron, which makes a folding polyhedron called a trapezoidal icosatetrahedron. This structure has been modified and implemented in a form of an imaging head of a hemispherical geometry. For many purposes of the instant invention, it is appropriate to use design features of smoothly varying surfaces based on the Hoberman concept of expanding structures. Depending on the implementation, other polygonal or spherical-type shapes may also be used with the principles of the present invention for other imaging head designs. Adjustment of the device in Figure 7 causes uniform expansion or contraction, thereby always preserving a hemispherical geometry. Imaging head **700** illustrates one example of modification to the "Hoberman" geometry. A receptacle for the fiber bundles **701** is disposed about imaging head **700**. Target volume **702** is where the medium would enter the imaging head in this implementation. This geometry is well suited for the investigation of certain tissues such as the female breast or the head. Depending on the implementation, attachment of optical fibers to the vertices of the hemisphere allows for up a seventeen (17) source by seventeen (17) detector measurement. The detectors or energy receivers may be disposed about the spherical imaging head and the detectors are located on the inner aspect of the expanding imaging head. Additional fiber bundles can be attached to the interlocking joints, permitting up to a 49 source by 49 detector measurement.

Depending on the implementation, light collected from the target medium is measured by using any of a number of optical detection schemes. One embodiment uses a fiber-taper, which is bonded to a charged coupled detector (CCD) array. The front end of the fiber taper serves to receive light exiting from the collection fibers. These fibers are preferably optical fibers, but can be any means that allows the transmission and reception of signals. The back end of the fiber taper is bonded to a 2-D charge-coupled-detector (CCD) array. In practice, use of this approach generally will require an additional signal attenuation module.

An alternate detection scheme employs an array of discrete photo detectors, one for each fiber bundle. This unit can be operated in a phase lock mode thereby allowing for improved rejection of ambient light signals and the discrimination of multiple simultaneously operated energy sources.

In another embodiment, in order to fulfill the demands posed by the desired physiological studies on the instrument, the following features characterize the detector system: scalable multi-channel design (up to 32 detector channels per unit); high detection sensitivity (below 10 pW); large dynamic range ($1{:}10^6$ minimum); multi-wavelength operation; ambient light immunity; and fast data acquisition (order of 100 Hz all-channel simultaneous capture rate).

To achieve this, the detector system uses photodiodes and a signal recovering technique involving electronic gain switching and phase sensitive detection (lock-in amplification) for each detector fiber (in the following referred to as detection or detector channels) to ensure a large dynamic range at the desired data acquisition rate. The phase sensitive signal recovery scheme not only suppresses electronic noise to a desired level

but also eliminates disturbances given by background light and allows simultaneous use of more than one energy source. Separation of signals from simultaneously operating sources can be achieved, as long as the different signals are encoded in sufficiently separated modulation frequencies. Since noise reduction techniques are based on the reduction of detection bandwidth, the system is designed to maintain the desired rate of measurements. In order to achieve a timing scheme that allows simultaneous readout of the channels, a sample-and-hold circuit (S/H) is used for each detection channel output. The analog signals provided by the detector channels are sampled, digitized and stored using the data acquisition system **116**. One aspect is the flexibility and scalability of the detection instrument. Not only are the detector channels organized in single, identical modules, but also the phase detection stages, each containing two lock-in amplifiers, are added as cards. In this way, an existing setup can easily be upgraded in either the number of detector channels and/or the number of wavelengths used (up to four) by cloning parts of the existing hardware.

FIG. 8 shows the block diagram of one implementation of a detector channel. In this implementation , two energy sources are being used. After detecting the light at the optical input **801** by a photo detector **802** the signal is fed to a transimpedance amplifier **803**. The transimpedance value of **803** is externally settable by means of digital signals **813** (PTA=Programmable Transimpedance Amplifier). This allows the adaptation to various signal levels thereby increasing the dynamic range of the detector channel. The signal is subsequently amplified by a Programmable Gain Amplifier (PGA) whose gain can be set externally by means of digital signals **814**. This allows for additional gain for

the lowest signal levels (e.g., in one implementation ~pW-nW) thereby thereby increasing the dynamic range of the detector channel.

In one embodiment, at least one energy source is used and the signal is sent to at least one of lock-in amplifiers (LIA) **805, 809**. Each lock-in amplifier comprises an input **808,812** for the reference signal generated by phase shifter **204** from FIG 2. After lock-in detection, the demodulated signal is appropriately boosted in gain by means of a programmable gain amplifier (PGA) **806, 810** in order to maximize noise immunity during further signal transmission and to improve digital resolution when being digitized. The gain of PGA **806, 810** is set by digital signals **815**.

At each output, a sample-and-hold circuit (S/H) **807, 811** is used for freezing the signal under digital timing by means of signal **816** for purposes described herein.

In one embodiment, the signal **815** is sent to **806, 810** in parallel. In one embodiment, the signal **816** is sent to **807, 811** in parallel.

As previously illustrated in FIG. 1, the analog signal provided by each of the channel outputs is sampled a data acquisition system **116**. In one embodiment, PC extension boards might be used for this purpose. PC extension boards also provide the digital outputs that control the timing of functions such as gain settings and sample-and-hold.

As previously noted, timing is crucial in order to provide the desired image capture rate and to avoid false readings due to detector-to-detector time skew. FIG. 9 shows one improvement of the invention over other timing schemes. With systems not comprising fast adaptable gain settings (such as some CCD based systems), a schedule according to **905** has to be implemented. The implementation in FIG 9 illustrates one use

of a silicon photo-diode in process **904**, which can be replaced by various detectors previously mentioned. A time series of data is acquired for a fixed source position. After finishing this task, the source is being moved **902** with respect to the target **901** and another series of data is being collected. Measurements are being performed in this fashion for all source positions. Every image **903** of the resulting time series of reconstructed images are being reconstructed from data sets merged together from the data for each source position. This schedule does not allow real-time capture of all physiologic processes in the medium and therefore only applies to certain modes of investigation. Although we are aware of the use of such schemes, e.g., when monitoring responses on repeatable maneuvers, the timing scheme for the invention very much improves on this situation.

Because the invention allows for fast source switching and large dynamic range and high data acquisition rates, a schedule indicated by **904** is performed. Here, the source position is switched fast compared to the dynamic features of interest and instantaneous multi-channel detection is performed at each source position. Images **903** are then reconstructed from data sets, which represent an instant state of the dynamic properties of the medium. Only one time series of full data sets (i.e., all source positions and all detector positions) is being recorded. Real time measurement of fast dynamics (e.g., faster 1 Hz) of the medium is provided by the invention.

FIG 10 shows one embodiment of a detailed schedule and sequence of the system tasks **1001** involved in collecting data at a source position and the proceeding of this process in time **1002**. Task **1003** is the setting of the optical de-multiplexer to a destined source position and setting the detectors to the appropriate gain settings. The source

position is illuminated for a period of time **1004**, during which the lock-in amplifiers settle **1005**. After the time it takes the S/H to sample the signal **1006**, the signal is being hold for a period of time **1007**, during which all channels are being read pout by the data acquisition. It is worthwhile noticing that during reading out the S/H, other tasks, like moving the optical source, setting the detector gains for the new source position, and settling of the lock-in, are being scheduled. This increases greatly the achievable data acquisition rate of the instrument.

This concept of a modular system is further illustrated in FIG. 11. Up to thirty-two (32) detector modules **1100** (each with 2 lock-in modules each for two modulation frequencies) are arranged using an enclosure **1102**. The cabinet also can carry up to two phase shifting modules **1104, 1106,** each containing two digital phase shifter under computer control. The ability to adjust the reference phase with respect to the signal becomes necessary since unavoidable phase shifts in the signal may lead to non-optimum lock-in detection or can even result in a vanishing output signal. Organization of data, power supply and signal lines is provided by means of two back planes **1108, 1110**

Depending on the implementation, the detector system design illustrated in FIG. 8 allows one cabinet to operate at a capacity of 32 detectors with four different sources requiring 128 analog to digital circuit (ADC)-board input channels. The upper **1108** and the lower **1110** back plane are of identical layout and have to be linked in order to provide the appropriate distribution of supply-, control- and signal voltages. This is achieved using a 6U-module fitting both planes from the backside, that provides the necessary electric linking paths, and interfaces for control- and signal lines.

FIG. 12 shows the schematic of one implementation of a channel module. In this implementation, a silicon photodiode 1206 is used as the photo-detector. A Programmable Transimpedance Amplifier (PTA) **1201** is formed by an operational amplifier **1204** , resistors **1201** and **1202** and an electronic switch **1205**, the latter of which is realized using a miniature relay. Other forms of electronic switches such as analog switches might be used. Relay **1205** is used to connect or disconnect 1203 from the circuit thereby changing the transimpedance value of **1201**. A high-pass filter (R2, C5) is used to AC-couple the subsequent programmable gain instrumentation amplifier **IC2** (Burr Brown PGA202) in order to remove DC offset. The board-to-board connectors for the two lock-in-modules are labeled as "slot A" **1210** and "slot B" **1212**. The main connector to the backplane is a 96-pole DIN plug **1220**.

FIG. 13, illustrates the electric circuit of the lock in modules **1210, 1212**. The signal is subdivided and passed to two identical lock-in-amplifiers, each of which gets one particular reference signal according to the sources used in the experiment. The signal is first buffered **IC1, IC7** (AD LF111) and then demodulated using an AD630 double-balanced mixer **IC2, IC8**.

In order to remove undesired AC components, the demodulated signal passes through an active 4-pole Bessel-type filter **IC3, IC4, IC 9, IC10** (Burr Brown UAF42). A Bessel-type filter has been chosen in order to provide fastest settling of the lock-in amplifier for a given bandwidth. Since a Bessel-filter shows only slow stopband-transition, a 4-pole filter is being used to guarantee sufficient suppression of cross talk between signals generated by different sources (i.e. of different modulation frequency). The filter has its 3 dB point at 140 Hz, resulting in 6 ms settling time for a step response

(<1% deviation of actual value). The isolation of frequencies separated by 1 kHz is 54 dB. The filters are followed by a programmable gain amplifier **IC5, IC 11**, whose general function has been described above. The last stage is formed by a sample-and-hold chip (S/H) **IC6, IC12** (National LF398).

In another implementation, the phase sensitive detection can be achieved with digital methods using digital signal processing (DSP) components and algorithms. The advantage of using DSP with the principles of the present invention is improved lectronic performance and enhanced system flexibility.

In another implementation, an analog-to-digital converter is used for each detector channel thereby improving noise immunity of the signals.

Although illustrative embodiments have been described herein in detail, those skilled in the art will appreciate that variations may be made without departing from the spirit and scope of this invention. Moreover, unless otherwise specifically stated, the terms and expressions used herein are terms of description and not terms of limitation, and are not intended to exclude any equivalents of the system and methods set forth in the following claims.

What is claimed is:

1. A system for use in tomographic imaging of a scattering medium, comprising:

an energy source for emitting a signal and having at least one energy transmitter coupled thereto; and

a detection system coupled to the energy source and including at least one energy receiver for measuring dynamic properties of the scattering medium.

2. The system of claim 1, further including an imaging head coupled as the energy transmitter and energy receiver for holding thereof.

3. The system of claim 1, wherein the detection system further comprises at least one lock-in amplifier for separating a signal emitted by at least one energy source.

4. The system of claim 1, wherein the detection system further includes at least one gain adjustment means for increasing dynamic range of the detector system.

5. The system of claim 1, wherein the detection system further includes a sample-and-hold circuit for freezing the signal emitted by the energy source.

6. The system of claim 5, wherein the sample-and-hold circuit further includes logic for allowing simultaneous readout for each detector fiber.

7. The system of clam 1, wherein the energy source includes at lest one of non-laser optical sources, LED and high-pressure incandescent lamp, laser diodes, solid state lasers, titanium-sapphire laser, ruby laser, dye laser, electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and combinations thereof.

8. The system of claim 1, wherein data acquisition from the detection system is about 150Hz.

9. The system of claim 1, wherein the energy source includes a plurality of near infra red laser diodes to transmit multiple wavelengths.

10. A detection system to collect data about the dynamic properties of a scattering medium, comprising:

at least one energy receiver for detecting a signal from an energy source; and

a programmable gain instrumentation amplifier for increasing the dynamic range of the signal which provides rapid data acquisition about the dynamic properties of the scattering medium.

11. The detection system of claim 10, wherein the energy receiver includes at least one of a photo-diode, PIN diode, Avalanche photodiodes , change couple device, change inductive device, photo-multiplier tubes, multi-channel plate, acoustic transducers, and any combinations thereof.

12. The detection system of claim 10, further including a sample-and-hold circuit coupled to the programmable gain instrumentation amplifier that allows simultaneous readout of a plurality of signals from the energy source.

13. A system for use in optical tomographic imaging of a scattering medium comprising:

at least one energy transmissive fiber bundle coupled to an energy source;

an imaging head for holding the energy transmissive fiber bundle; and

a detection system for collecting data about the optical dynamic properties of the scattering medium.

14. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

15. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

16. The system of claim 13, wherein the imaging head is a folding sphere or polygon.

17. The system of claim 16, wherein the polygon is a polyhedron or a trapezoidal icosatetrahedron, or a hemitrapezoidal icosatetrahedron..

18. The system of claim 16, wherein the fiber bundle is disposed about the imaging head.

19. The system of claim 13 wherein the fiber bundle has a diameter of about 3 mm.

20. The system of claim 13, wherein the imaging head further includes adjustment means for accommodating different size medium, stabilizing the medium against motion artifacts, conforming the target to a simple well-defined geometry and

providing information about the location of at lest the receiver in reference to the location of the transmitter.

21. A method of using optical tomographic imaging, comprising:

(a) exposing a scattering medium to near infra-red light; for collecting data about the dynamic properties of a scattering medium,

(b) detecting light by a detection system; and

(c) enhancing gain through a programmable gain instrumentation amplifier for the purpose of measuring the dynamic properties of the scattering medium.

22. The method of claim, wherein the scattering medium is vascular tissues.

23. The method of claim 21, further including separating via at least one lock-in amplifier a plurality of wavelengths transmitted through the medium.

24. The method of claim 21, further including collecting data from simultaneous readouts of a signal.

25. A system for optical tomographic imaging of a medium comprising:

an imaging head having at least one source disposed to direct optical energy into a medium and a plurality of detectors disposed to receive optical energy emerging from the medium, the detectors means being located at a plurality of distances from the source constituting a plurality of distances through the medium the detectors and thee source , the source and detectors forming respective source detector pairs;

a programmable gain amplifier connected to amplify at least one signal of the source detector pairs;

a computer having a data acquisition board for receiving the signal from the programmable gain amplifier and reconstructing an image of the medium.

26. The system of claim 25, wherein the optical energy comprises optical energy of at least two different intensity modulated wavelengths of energy.

27. The system of claim 26, further comprising a filtering means for separating signals corresponding to a wavelength of intensity modulated energy.

28. The system of claim 25, further comprising a sample and hold circuit for holding a desired signal for use in measuring of dynamic properties of the medium.

29. The system of claim 25, wherein the source comprises energy transmissive fibers coupled to an energy emitting source.

30. The system of claim 25, wherein the source comprises a plurality of optical energy sources.

31. The system of claim 25, wherein the source comprises of plurality of laser diodes.

32. The system of claim 25, wherein the detectors are fibers coupled to optical energy detectors.

33. The system of claim 25, wherein the detectors are optical energy detectors.

34. An imaging head comprising

a pad;

a plurality of source means for delivering optical energy to a medium; and

a plurality of detector means for detecting optical energy emerging from a medium, the source means and detector means being attached to the pad in a plurality of rows and columns wherein the plurality of source means are arranged to form at least two unique imaging planes, an imaging plane being between defined by a plane substantially perpendicular to the pad and passing through at least two source means and one detector means.

35. The imaging head of claim 34, wherein a plurality of source means and detector means are joined to form combined source detector means, the combined source detector means and detector means being arranged in an alternating rows of a first pattern and a second pattern, the first pattern comprising one combined source detector means followed by three detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means, the second pattern comprising two detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means followed by two detector means.

36. The imaging head of claim 34, wherein the source means are fibers coupled to an optical energy source.

37. The imaging head of claim 34, wherein the source means are optical energy sources.

38. The imaging head of claim 34, wherein the source means is laser diodes.

39. The imaging head of claim 34, wherein the detector means are fibers coupled to optical energy detectors.

40. The imaging head of claim 34 wherein the detector means are optical energy detectors.

41. The imaging head of claim 34 wherein the detector means are photodiodes.

42. An adjustable imaging head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements, each trust element having a central pivot point, an internal terminal pivot point and an external terminal pivot point that do not lie on a straight line, each strut being pivotally joined to the other of its pair by their central pivot points, each strut being pivotally joined by the internal terminal pivot point and the external terminal pivot point to the internal terminal pivot point and the external terminal pivot point respectively of another scissors pair, whereby an adjustable ring of principle vertices is formed by the internal terminal pivot points and whereby adjustment causes uniform movement of the principle vertices, the improvement comprising:

at least one source means for delivering optical energy into a medium and at least one detector means for detecting optical energy emerging from a medium, wherein the source means and the detector means are attached to the principle vertices, the source means being oriented to direct optical energy substantially toward a medium in

the center of the ring, the detector means being oriented to receive optical energy emerging substantially from a medium in the center of the ring.

43. The adjustable imaging head of claim 42, further comprising:

amount in communication with a truss element, wherein the mount supports the imaging head and regulates the size of the adjustable ring.

44. The adjustable imaging head of claim 42, further comprising:

a first set of mounts in communication with a first set of diametrically opposed external terminal pivot points;

a second set of mounts in communication with a second set of diametrically opposed external terminal pivot points, wherein the first set of diametrically opposed external terminal pivot points is orthogonal to the second set of diametrically opposed external terminal pivot points,

a drive system in communication with at least one of the mounts in at least one of the first or second sets of mounts, whereby the drive system regulates the size of the adjustable ring.

45. The imaging head of claim 42, wherein the source means are fibers coupled to an optical energy source.

46. The imaging head of claim 42, wherein the source means are optical energy sources.

47. The imaging head of claim 42, wherein the source means are laser diodes.

48. The imaging head of claim 42, wherein the detector means are fibers coupled to optical energy detectors.

49. The imaging head of claim 42, wherein the detector means are optical energy detectors.

50. The imaging head of claim 42, wherein the detector means are photodiodes.

51. An imaging head for use in optical tomography, comprising:

at least one energy receiver;

adjustment means for accommodating different sizes of the medium; and

communication means for transmitting signals from the imaging head to a detection system for use in the measurement of dynamic properties of a scattering medium.

52. The imaging head of claim 49, further including at least one energy transmitter.

53. The imaging head of claim 52, wherein the energy transmitters define an illumination array configured to minimize subsequent numerical effort required for data analysis and maximizing source density covered by the array.

54. The imaging head of claim 53, wherein three dimensional images can be computed from super positioning of the array of two dimensional images.

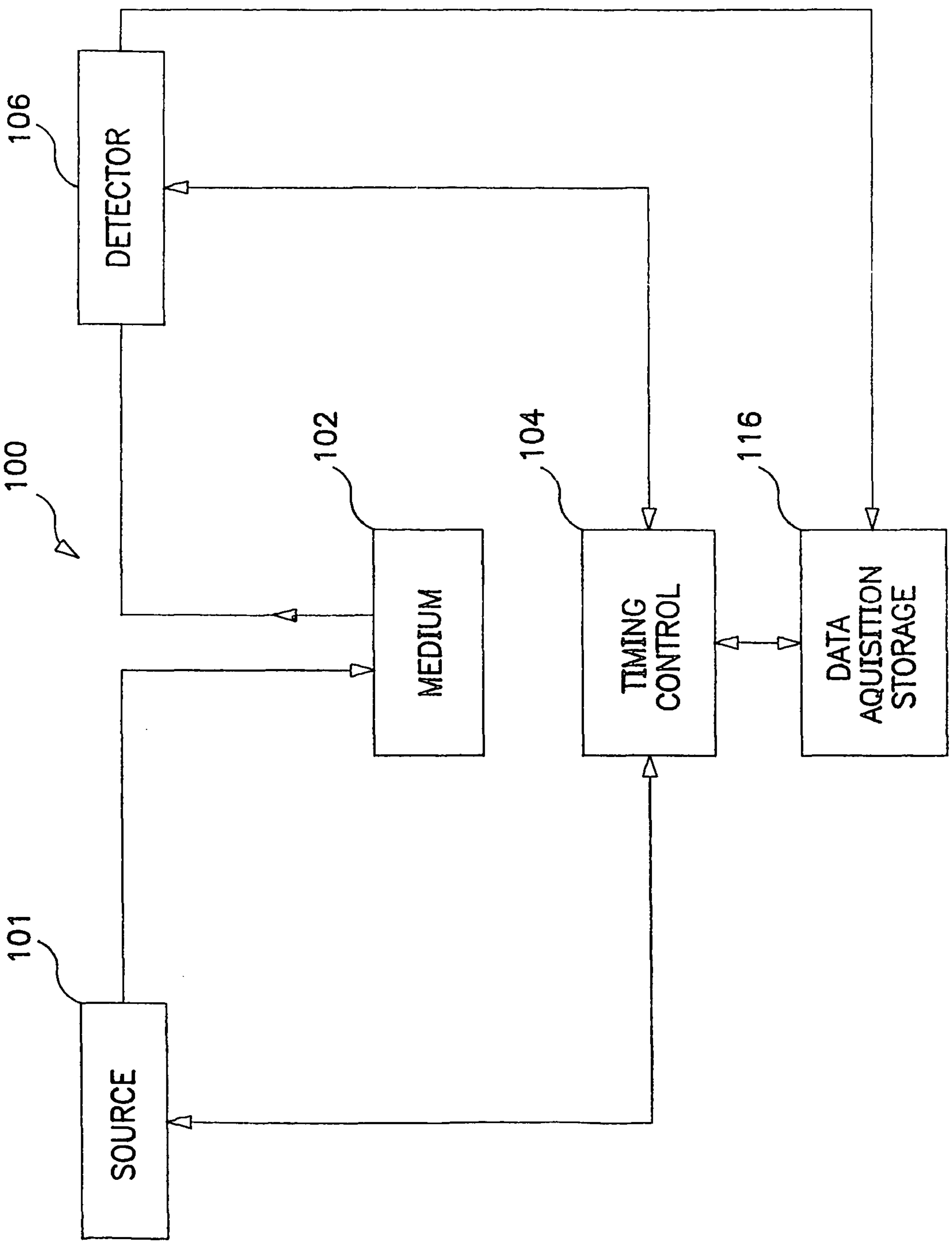
100
101
SOURCE
102
MEDIUM
104
TIMING
CONTROL
106
DETECTOR
116
DATA
AQUISITION
STORAGE

FIG. 1

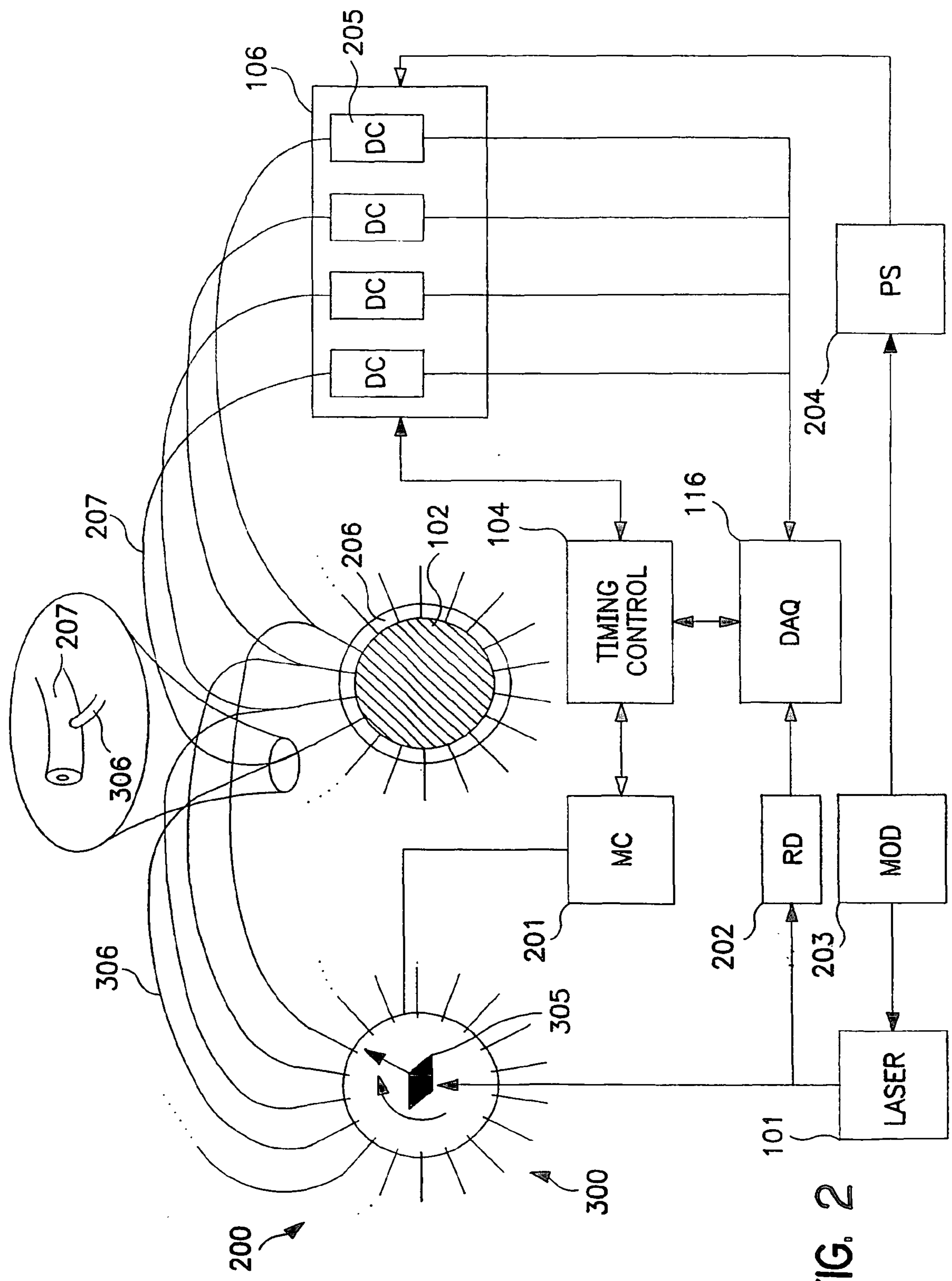
106
205
DC
DC
DC
DC
PS
204
207
206
102
104
116
TIMING CONTROL
DAQ
207
306
MC
RD
MOD
201
202
203
306
305
LASER
101
300
200

FIG. 2

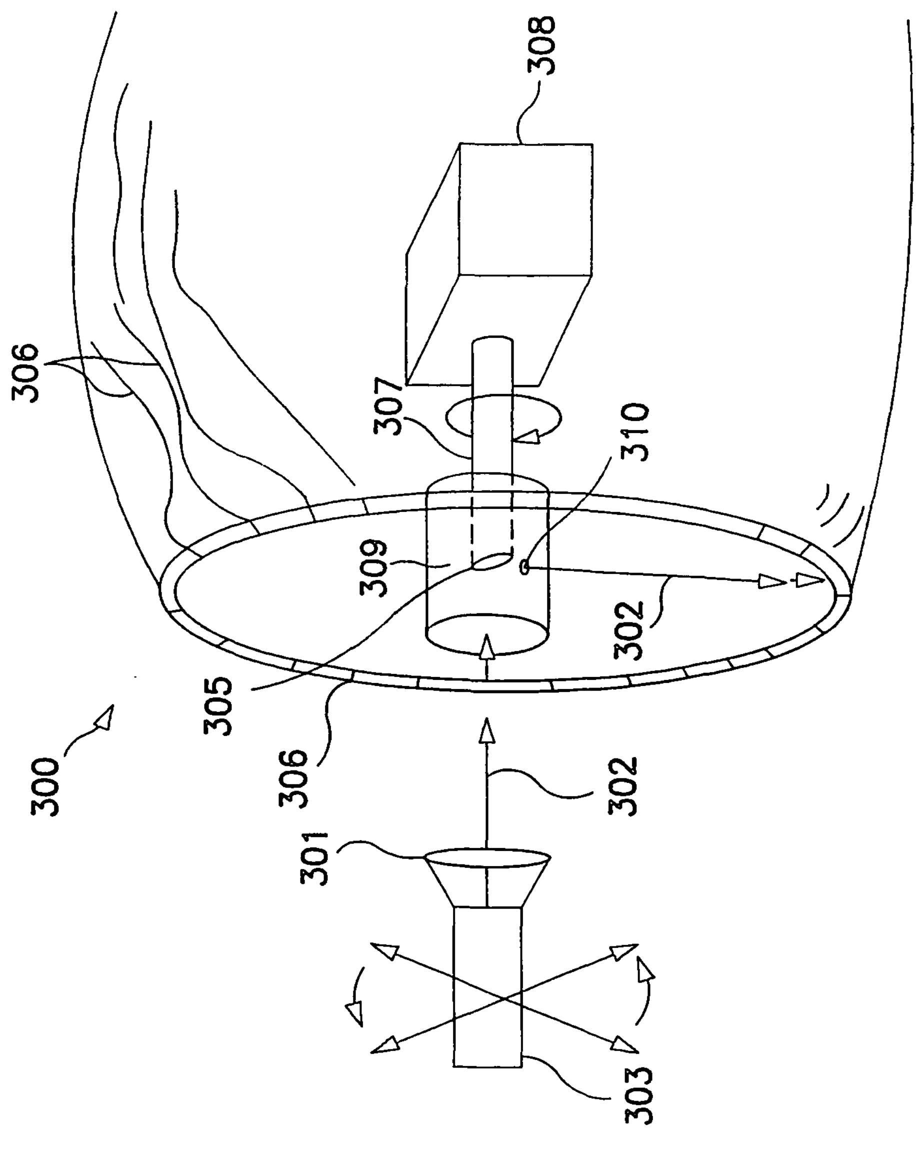

FIG. 3

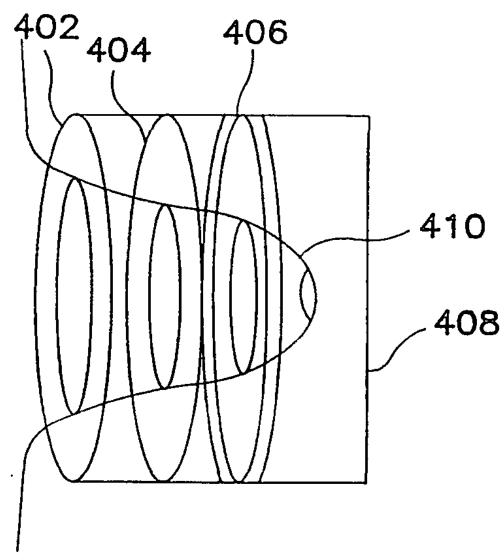

FIG. 4

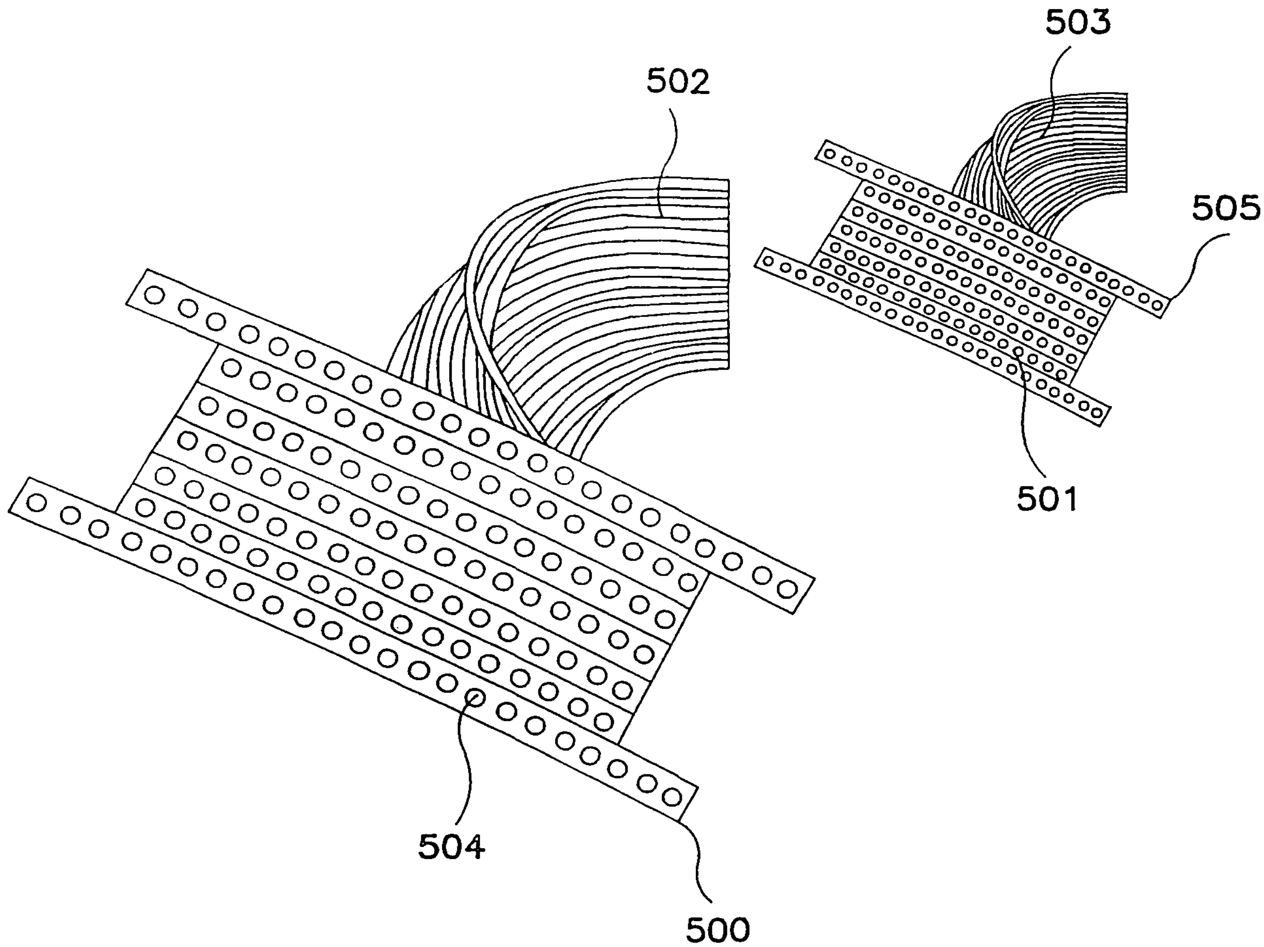

FIG. 5

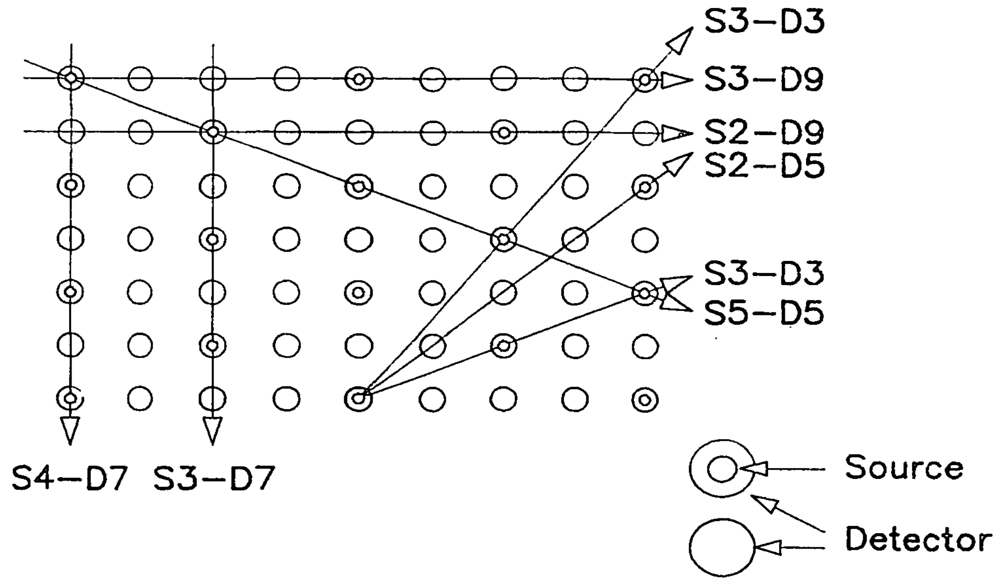

FIG. 6

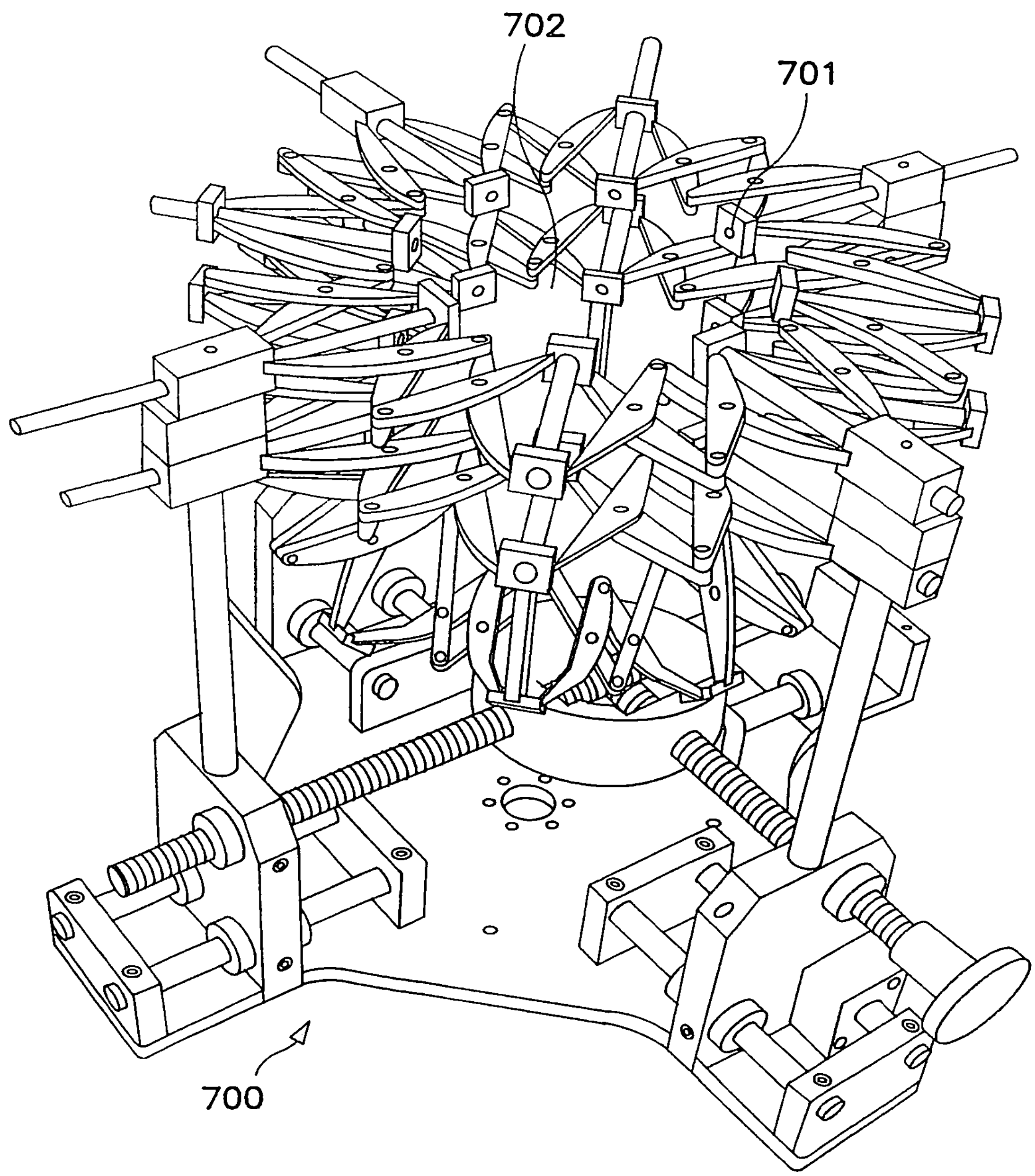

FIG. 7

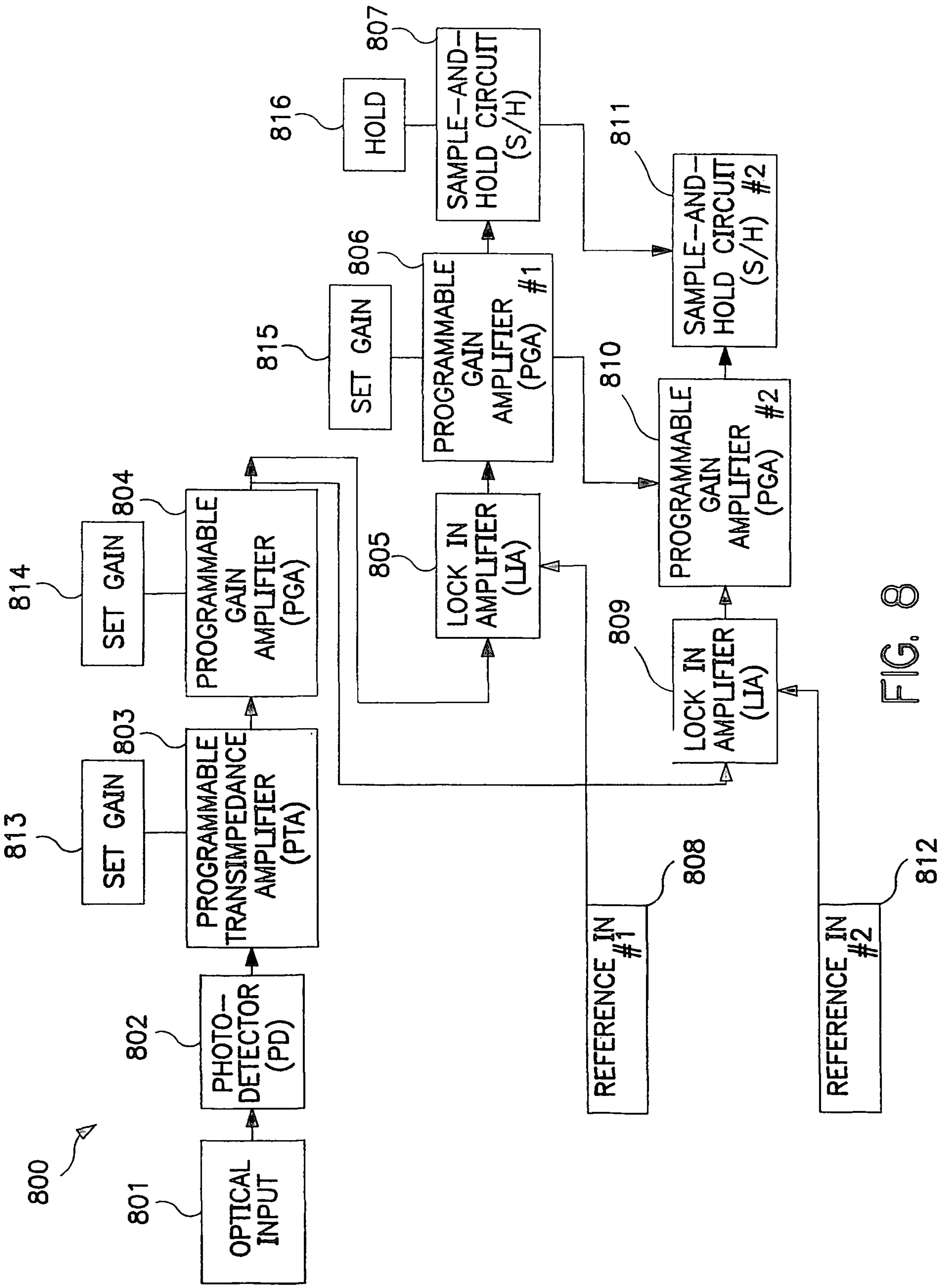
800
801
OPTICAL INPUT
802
PHOTO-DETECTOR (PD)
803
PROGRAMMABLE TRANSIMPEDANCE AMPLIFIER (PTA)
813
SET GAIN
804
PROGRAMMABLE GAIN AMPLIFIER (PGA)
814
SET GAIN
805
LOCK IN AMPLIFIER (LIA)
806
PROGRAMMABLE GAIN AMPLIFIER (PGA) #1
815
SET GAIN
807
SAMPLE-AND-HOLD CIRCUIT (S/H)
816
HOLD
808
REFERENCE IN #1
809
LOCK IN AMPLIFIER (LIA)
810
PROGRAMMABLE GAIN AMPLIFIER (PGA) #2
811
SAMPLE-AND-HOLD CIRCUIT (S/H) #2
812
REFERENCE IN #2

FIG. 8

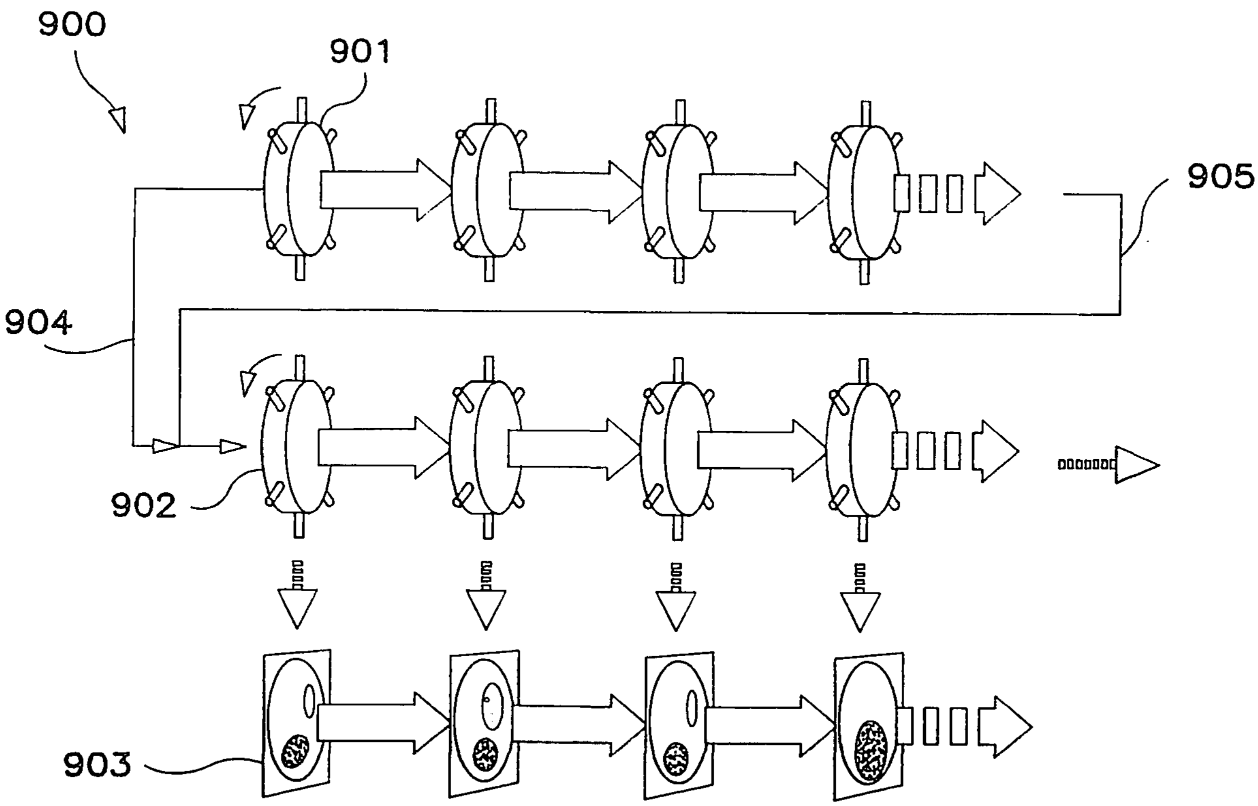

FIG. 9

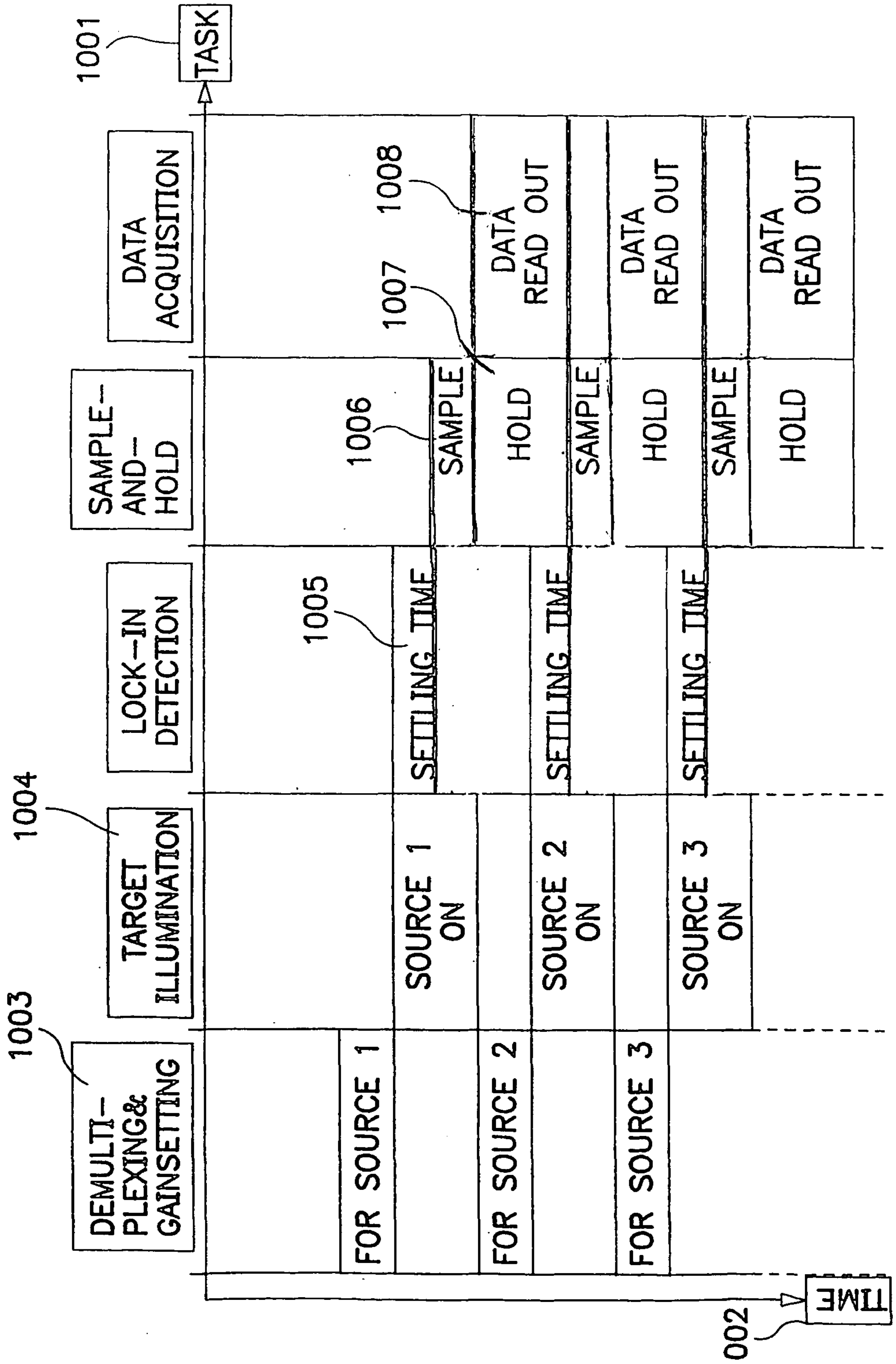
TASK
1001
DEMULTI-PLEXING& GAINSETTING
1003
TARGET ILLUMINATION
1004
LOCK-IN DETECTION
SAMPLE-AND-HOLD
DATA ACQUISITION
FOR SOURCE 1
SOURCE 1 ON
1005
SETTLING TIME
1006
SAMPLE
1007
HOLD
1008
DATA READ OUT
FOR SOURCE 2
SOURCE 2 ON
SETTLING TIME
SAMPLE
HOLD
DATA READ OUT
FOR SOURCE 3
SOURCE 3 ON
SETTLING TIME
SAMPLE
HOLD
DATA READ OUT
TIME
1002

FIG. 10

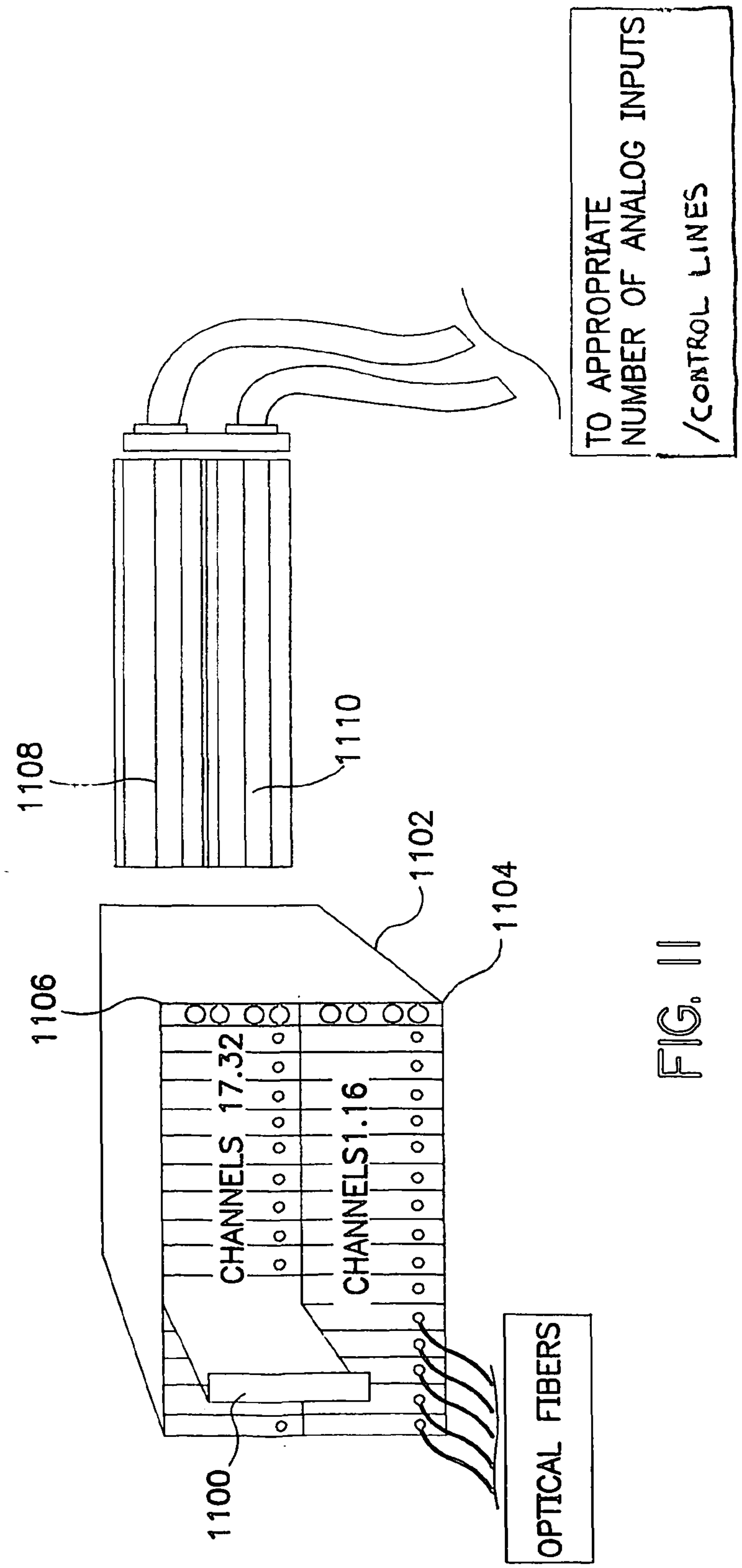
TO APPROPRIATE
NUMBER OF ANALOG INPUTS
/CONTROL LINES
1108
1110
1102
1104
1106
CHANNELS 17.32
CHANNELS1.16
OPTICAL FIBERS
1100

FIG. 11

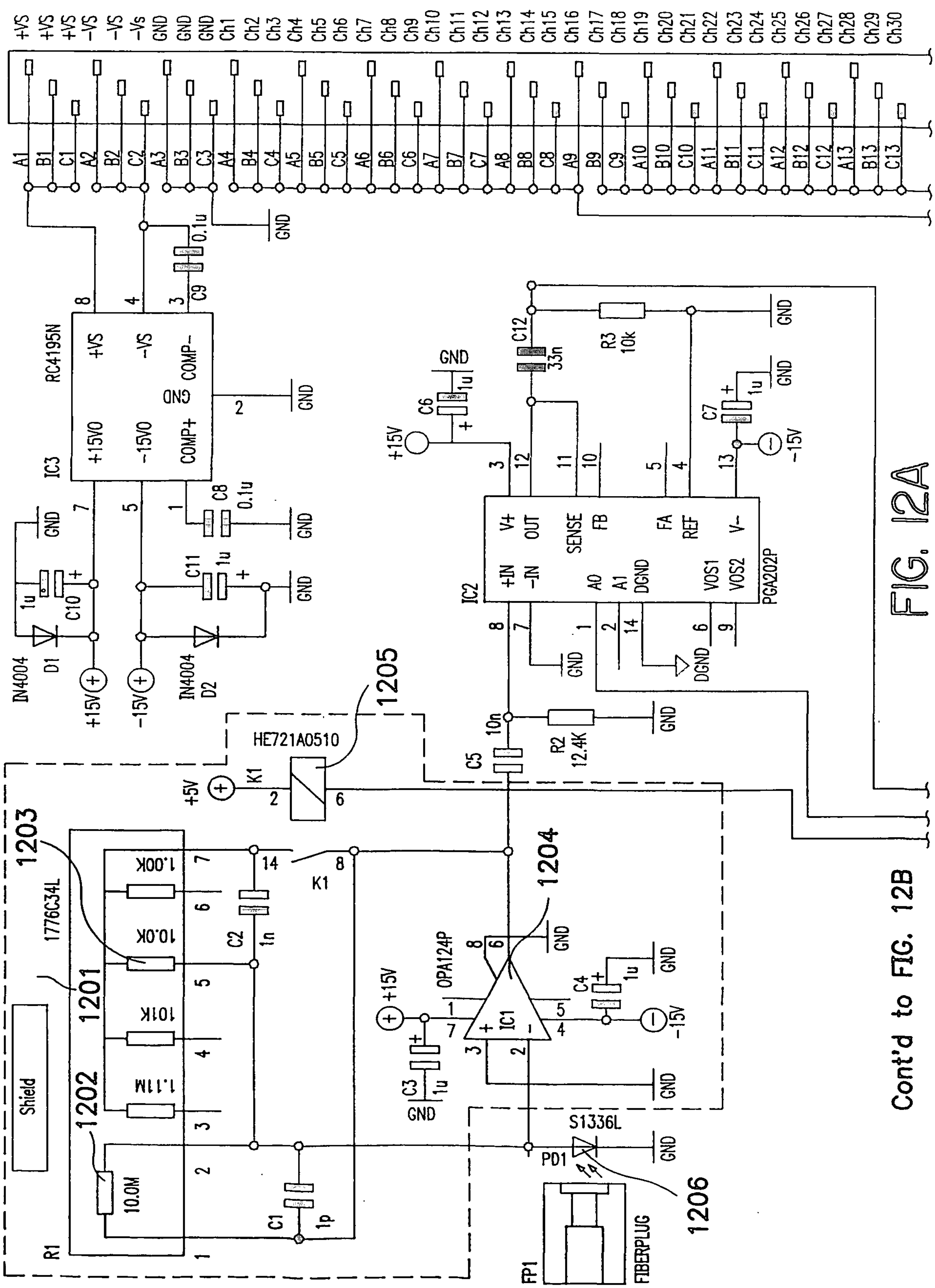

FIG. 12A

Cont'd to FIG. 12B

Cont'd from FIG. 12A

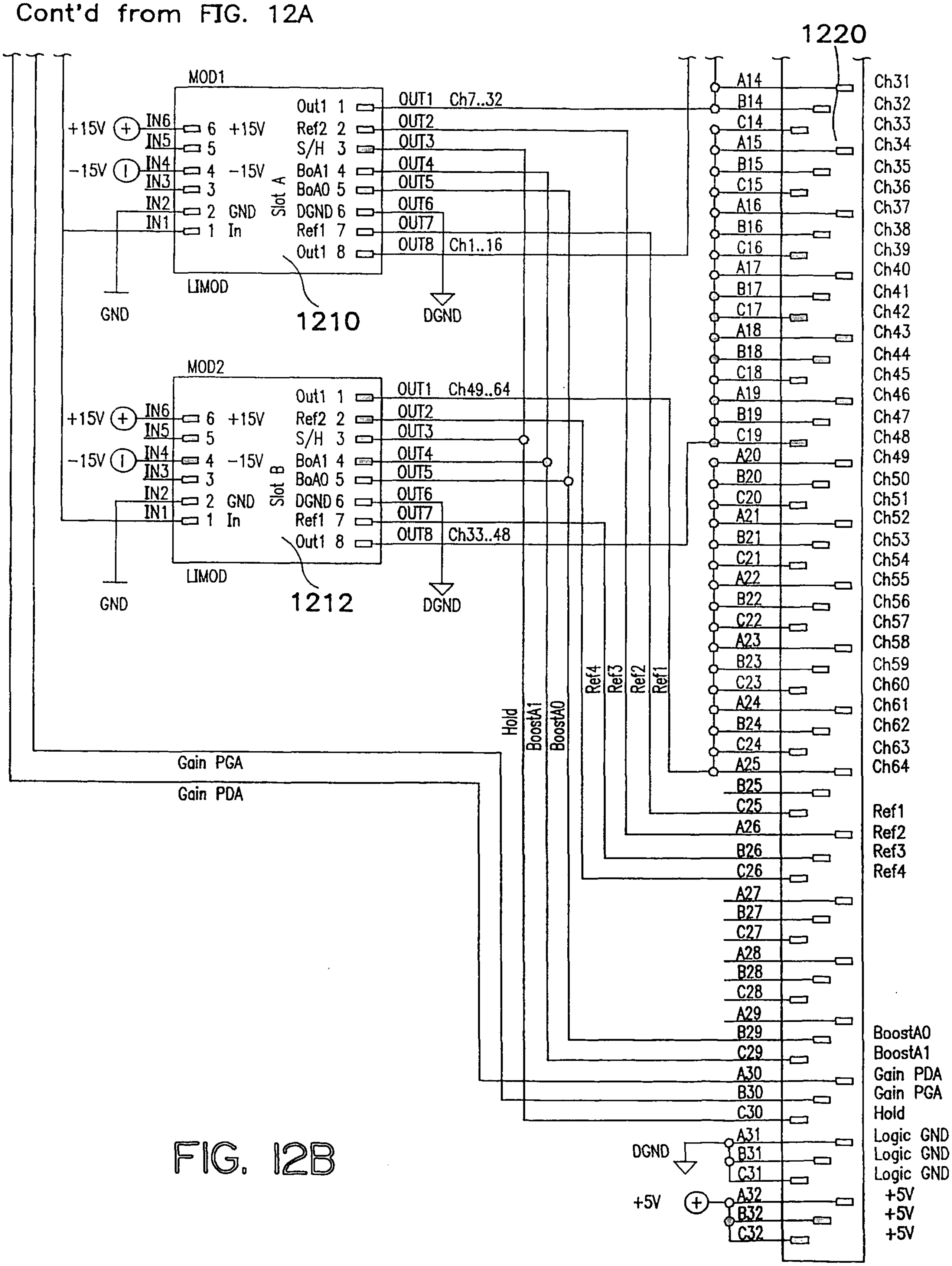

FIG. 12B

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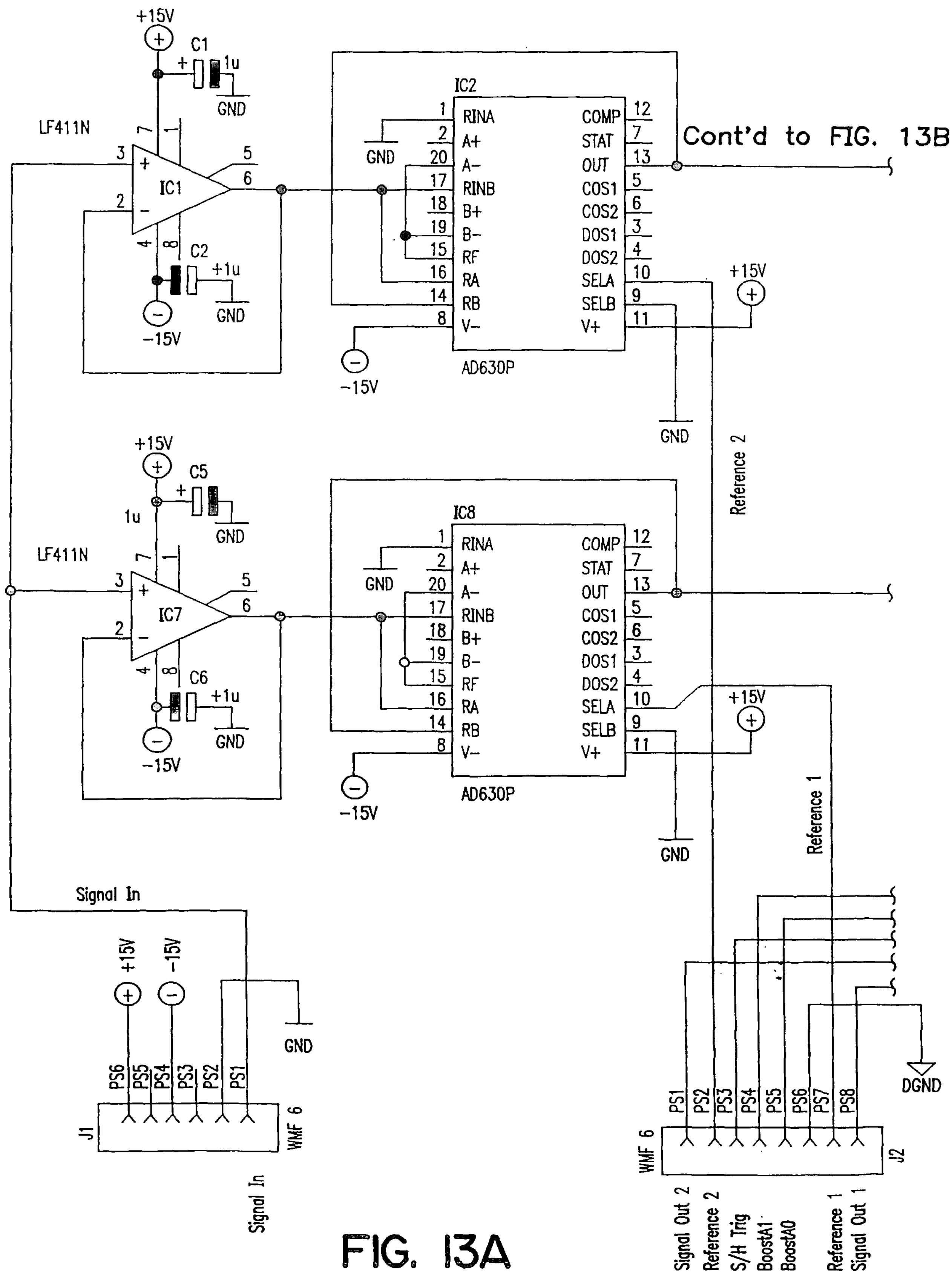

+15V
C1
1u
GND
LF411N
IC1
C2
+1u
-15V
IC2
RINA
A+
A-
RINB
B+
B-
RF
RA
RB
V-
COMP
STAT
OUT
COS1
COS2
DOS1
DOS2
SELA
SELB
V+
AD630P
Cont'd to FIG. 13B
Reference 2
C5
IC7
C6
IC8
Reference 1
Signal In
J1
WMF 6
PS1
PS2
PS3
PS4
PS5
PS6
PS7
PS8
DGND
J2
Signal Out 2
Reference 2
S/H Trig
BoostA1
BoostA0
Reference 1
Signal Out 1

FIG. 13A

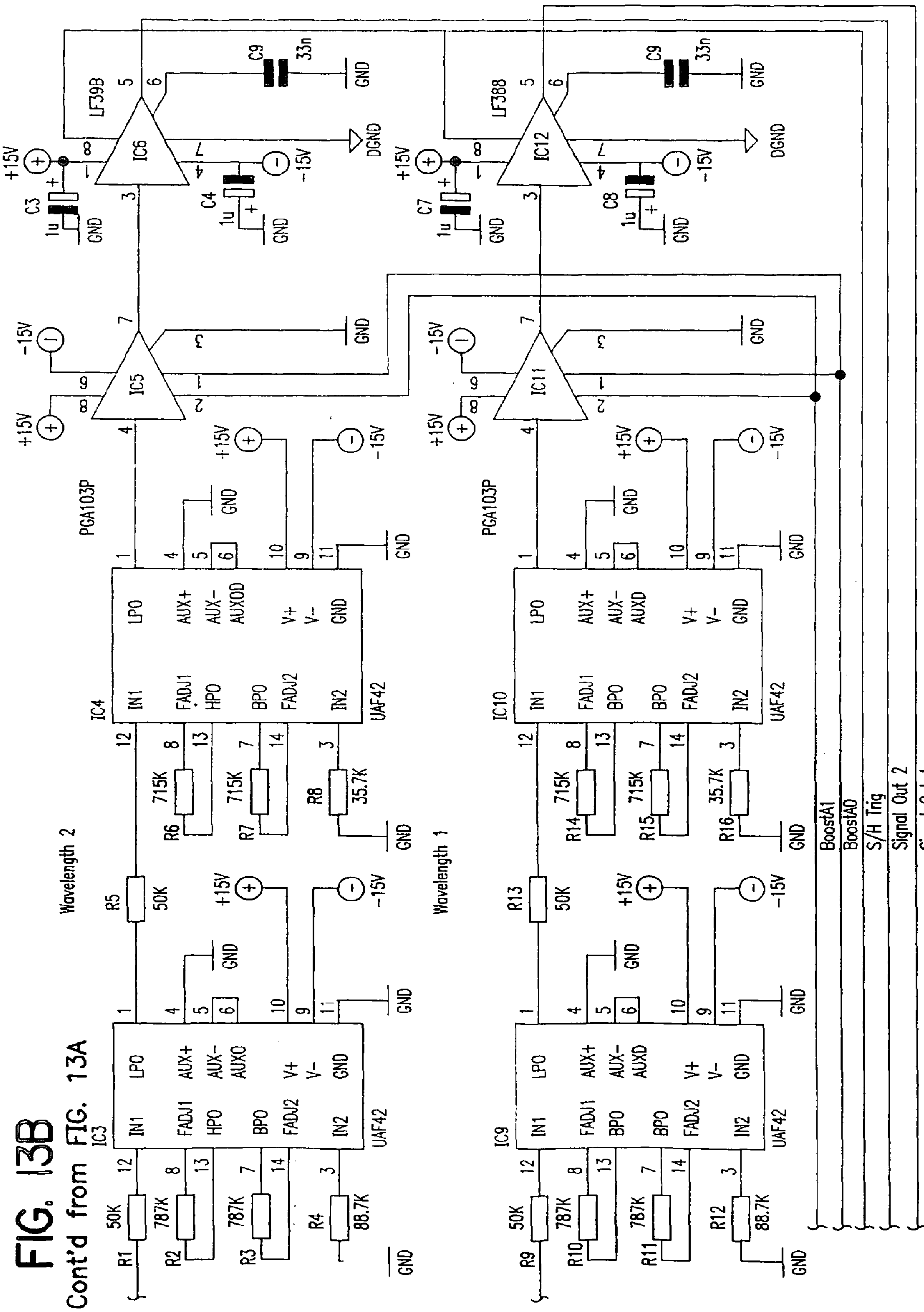

FIG. 13B
Cont'd from FIG. 13A

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/25155

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :G01N 21/00; H01J 3/14
US CL :356/436; 250/216
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/436; 250/216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPTO EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P ---- A	US 5,994,690 A (Kulkarni et al) 30 November 1999, see entire document.	1-3,7,13,14,19 ----- 4-6,8-12,15-18,20-54

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
02 NOVEMBER 2000	09 JAN 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MICHAEL P. STAFIRA Telephone No. (703) 308-4837

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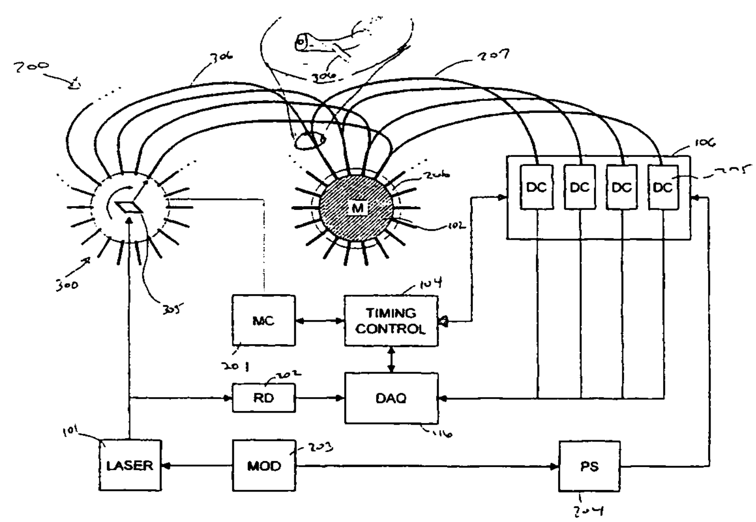
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

[Continued on next page]

(54) Title: SYSTEM AND METHOD FOR TOMOGRAPHIC IMAGING OF DYNAMIC PROPERTIES OF A SCATTERING MEDIUM



(57) Abstract: A system and method for the detection and three dimensional imaging of absorption and scattering properties of a medium such as human tissue is described. According to one embodiment of the invention, the system directs optical energy toward a turbid medium from at least one source and detects optical energy emerging from the turbid medium at a plurality of locations uisng at least one detector (106). The optical energy emerging from the medium (102) and entering the detector (106) originates from the source (101) is scattered by the medium (102). The system then generates an image representing interior structure of the turbid medium based on the detected optical energy emerging from the medium (102). Generating the image includes a time-series analysis.

WO 01/20306 A1

— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

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13/prts

SYSTEM AND METHOD FOR TOMOGRAPHIC IMAGING OF DYNAMIC PROPERTIES OF A SCATTERING MEDIUM

This invention was made with U.S. Government support under contract number CA-RO166184-02A, awarded by the National Cancer Institute. The U.S. Government has certain rights in the invention.

This application claims the benefit under 35 U.S.C. §120 of prior U.S. Provisional Patent Application Serial Nos. 60/153,926 filed September 14, 1999, entitled DYNAMIC TOMOGRAPHY IN A SCATTERING MEDIUM and 60/154,099 filed September 15, 1999, entitled DYNAMIC TOMOGRAPHY IN A SCATTERING MEDIUM.

This application is related to copending application serial number "not yet assigned", attorney docket number 0887-4147PC2, filed on the same date as this application, entitled "METHOD AND SYSTEM FOR IMAGING THE DYNAMICS OF SCATTERING MEDIUM" by inventor R. Barbour is hereby incorporated by reference (hereinafter the "Barbour 4147PC2 application").

This application is also related to copending application serial number "not yet assigned", attorney docket number 0887-4149PC1, filed on the same date as this application, entitled "METHOD AND SYSTEM FOR ENHANCED IMAGING OF A SCATTERING MEDIUM" by inventors R. Barbour and Y Pei and is hereby incorporated by reference (hereinafter the "Barbour 4149PC1 application").

This application is also related to copending application serial number "not yet assigned", attorney docket number 0887-4149PC2, filed on the same date as this application, entitled "IMAGING OF SCATTERING MEDIA USING RELATIVE DETECTOR VALUES" by inventor R. Barbour and is hereby incorporated by reference (hereinafter the "Barbour 4149PC2 application").

Field of the Invention

The invention relates to a system and method for tomographic imaging of dynamic properties in of a scattering medium, which may have special application to medical imaging, and in particular to systems and methods for tomographic imaging using near infrared energy to image time variations in the optical properties of tissue.

Background of the Invention

Contrary to imaging methods relying on the use of ionizing radiation and/or toxic/radioactive contrast agents, near infra-red (NIR)-imaging methods bear no known risk of causing harm to the patient. The dose of optical intensity used remains far below the threshold of thermal damage and is therefore safe. In the regime of wavelength/ intensity/power used, there are no effects on patient tissue that accumulate with increasing NIR dose due to over-all irradiation time.

The general technology involved in optical tomography is developed and understood, so that, compared to other cross-sectional imaging techniques such as MRI, X-ray CT, and the like, only moderate costs and relatively small-sized devices are required. Optical tomography especially gains from the development of small, economical, yet powerful semiconductor lasers (laser diodes) and the availability of highly integrated, economical off-the-shelf data processing electronics suitable for the application. Moreover, the availability of powerful yet inexpensive computers contributes to the attractiveness of optical tomography since a significant computational effort may be necessary for both image reconstruction and data analysis.

Optical tomography yields insights into anatomy and physiology that are unavailable from other imaging methods, since the underlying biochemical activities of

physiological processes almost always leads to changes in tissue optical properties. For example, imaging blood content and oxygenation is of interest. Blood shows prominent absorption spectra in the NIR region and vascular dynamics and blood oxygenation play a major role in physiology/pathology.

However, cross-sectional or volumetric imaging of dynamic features in large tissue structures is not extractable with current optical imaging methods. At present, whereas a variety of methods involving imaging and non–imaging modalities are available for assessing specific features of the vasculature, none of these assess measure dynamic properties based on measures of hemoglobin states. For instance, detailed images of the vascular architecture involving larger vessels (> 1 mm dia.) can be provided using x–ray enhanced contrast imaging or MR angiography. These methods however are insensitive to hemoglobin states and only indirectly provide measures of altered blood flow. The latter is well accomplished, in the case of larger vessels, using Doppler ultrasound, and for near–surface microvessels by laser Doppler measurements, but each is insensitive to variations in tissue blood volume or blood oxygenation. Ultrasound measurements are also limited by their ability to penetrate bone. Other methods are available, (*e.g.*, pulse volume recording, magnetic resonance (MR) BOLD method, radioscintigraphic methods), and each is able to sample, either directly or indirectly, only a portion of the indicated desired measures.

Thus, there is a need for a system and method of data collection providing cross-sectional or volumetric imaging of dynamic features in large tissue structures.

SUMMARY OF THE INVENTION

The present invention provides a system and method for generating an image of dynamic properties in a scattering medium. The system includes an energy source, such as a NIR emitting source, and a detection system to measure received energy. In an exemplary embodiment, the detection system has at least one photo-detector such as a photodiode, a means for rapid adjustment of signal gain, and a device for retaining a measured response in order to investigate the dynamic variations in the optical properties of tissues. Depending on the implementation, the detection system further may also include at least one means for separating a plurality of signals from the photo-receiver when multiple energy sources are used simultaneously. This simultaneous use of multiple energy sources allows the use of different wavelengths and/or different source locations at the same time.

In one implementation using optical tomographic imaging, a specimen is exposed to NIR light emitted from at least one laser diode. Furthermore an imaging head may be utilized that contains means for positioning at least one source location and / or at least one detector location with respect to the medium. The energy detector may use an energy collecting element, such as an optical fiber to transmit the received energy. The energy detector is responsive to the energy or light emerging from the specimen. In accordance with the invention, the signal from the detector is selectively enhanced in gain to increase the dynamic measurement range. The method may further include separating via at least one lock-in amplifier a plurality of signals generated by multiple energy sources. In addition, the method allows simultaneous measurements of signals produced by the NIR light by means of a sample-and-hold circuit when more than one detector fiber is used.

BRIEF DESCRIPTION OF THE FIGURES

For a better understanding of the invention, together with the various features and advantages thereof, reference should be made to the following detailed description of the preferred embodiments and to the accompanying drawings wherein:

FIG. 1 is a block diagram of one embodiment of a system according to the invention;

FIG. 2 is a block diagram illustrating one implementation of the system in FIG. 1;

FIG. 3 is a perspective view of a servo-motor apparatus useful in this invention to illuminate a number of fiber bundles with a single energy source;

FIG. 4 is a schematic illustration of the disposition for examining human tissue such as a human breast;

FIG. 5 is a photograph of a planar imaging head useful in one embodiment of the invention;

FIG. 6 is one embodiment for the source detector arrangement on the imaging head shown in FIG. 5;

FIG. 7 is an illustration of a spherical imaging head useful in practicing the invention;

FIG. 8 is a block diagram of a detector channel useful in practicing the invention;

FIG. 9 is a graphical representation of one implementation of a timing scheme used in the system of FIG.1;

FIG. 10 is a diagram illustrating the sequence of certain events in a multiple channel embodiment of the invention;

FIG. 11 is a schematic illustration of the physical arrangement of multiple detector channels used in a preferred embodiment of the invention;

FIG. 12 is a circuit diagram of one detector channel used in FIG. 11; and

FIG. 13 is a circuit diagram of one implementation of the lock-in module used in FIG 12.

DETAILED DESCRIPTION OF THE INVENTION

The objective of the invention is to provide a system and method capable to extract dynamics in properties of a scattering medium. The use of the invention's system and method has several applications including, but not limited to, medical imaging applications. Although the methods described herein focus on tomographic imaging the dynamic properties of hemoglobin states and tissue using optical tomography, with an imaging source generating multiple wavelengths in the NIR region, it is appreciated that the invention is applicable to any medium that is able to scatter the propagating energy from any energy source, including external energy sources such as those sources located outside the medium and/or internal sources such as those energy sources located inside the medium. For example, other media includes, but are not limited to, medium from mammals, botanical life, aquatic life, or invertebrates; oceans or water masses; foggy or gaseous atmospheres; earth strata; industrial materials; man-made or naturally occurring chemicals and the like. Energy sources include, but are not limited to, non-laser optical sources like LED and high-pressure incandescent lamps and lasers sources such as laser diodes, solid state lasers such as titanium-sapphire laser and ruby laser, dye laser and

other electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and any combinations thereof.

Similarly the means to detect the signal produced by the energy source is not limited to photodiode implementation discussed in one of the preferred embodiments further described herein. Other detectors can be used with the principles of the present invention for the purpose of tomographic imaging the dynamic properties of a medium. Such detectors include for example, but are not limited to, photo-diodes, PIN diodes (PIN), Avalanche Photodiodes (APD), charge couple device (CCD), charge inductive device (CID), photo-multiplier tubes (PMT), multi-channel plate (MCP),acoustic transducers and the like.

The present invention builds upon previous disclosures in U.S. Patent Nos. 5,137, 355 ("the '355 patent") entitled "Method of Imaging a Random Medium" ("the '355 patent") and 6,081,322 ("the '322 patent") entitled "NIR Clinical Opti-Scan System", the disclosures of both the '355 and '322 patents are incorporated herein by reference. Disclosed in these patents is an approach to optical tomography, and the instrumentation required to accomplish the tomography. The modifications in the present invention provide fast data acquisition, and new imaging head designs. Fast data acquisition allows accurate sampling of dynamic features. The modification in the imaging head allows accommodation of different size targets (e.g., breast); the stabilization of the target against motion artifacts; conforming the target to a simple well-defined geometry; and knowledge of source and detector positioning on or about the target. All of the enumerated features listed above for the imaging head is crucial for accurate image reconstruction.

Additionally, the present invention uses detector circuitry that allows quick adaptation of the measurement range to the signal strength thereby increasing the over-all dynamic range. "Dynamic range" for the purposes of this description means the ratio between the highest and lowest detectable signal. This makes the circuitry suitable for use with source-detector distances that can vary significantly during the data collection, thereby allowing fast data acquisition over wide viewing angles. For instance, we are aware that dynamic features of dense scattering media may be extractable from measurements using a single source and single detector at a fixed distance between each other. Depending on the implementation, such an arrangement could be made using a detector of relatively small dynamic range. Although we are aware of the possible usefulness of such a measurement, our invention allows the measurement of dynamics in optical properties of dense scattering media using source-detector pairs over a wide range of distances (e.g., greater than or about 5 cm). Such full tomographic measurements allow for improved accuracy in image reconstruction.

Depending upon the implementation, it is within the scope of the present invention to include those embodiments using a restricted source detector distance and therefore not requiring fast gain adjustment. For example, in one embodiment, the system of the present invention can also be operated using detector channels of low-dynamic range (e.g., 1:1000) when detector fibers of a fixed distance from the source are being used for the measurement (e.g., the detector opposite the source).

The data collection scheme of the present invention disclosed herein provides time-series of raw data sets that provide useful information about dynamic properties of the scattering medium without any further image reconstruction. For example, by

displaying the raw data in a color mapping format, features can be extracted by sole visual inspection. In addition to that, analysis algorithms of various types such as, but not limited to, linear and non-linear time-series analysis or pattern recognition methods can be applied to the series of raw data. The advantage of using these analytical methods is the improved capability to reveal dynamic signatures in the signals.

In another implementation, image reconstruction methods may be applied to the sets of raw data thereby providing time series of cross-sectional images of the scattering medium. For these implementations, analysis methods of various types such as, but not limited to, linear and non-linear time-series analysis, filtering, or pattern recognition methods can be applied. The advantage of using such analysis is the improved extraction of dynamic features and cross-sectional view, thereby increasing diagnostic sensitivity and specificity. These methods are explained in detail in the '355 and '322 patents, which were previously described and incorporated in as reference.

The invention reveals measurements of real-time spatial temporal dynamics. Depending on the implementation, an image of dynamic optical properties of scattering medium such as, but not limited to, the vasculature of the human body in a cross-sectional view is provided. The technology employs low cost, compact instrumentation that uses non-damaging near infrared optical sources and features several alternate imaging heads to permit investigation of a broad range of anatomical sites.

In another implementation, the principles of the present invention can be used in conjunction with contrast agents such as absorbing and fluorescent agents. In another variant, the present invention allows the cross-sectional measurements of changes in

optical properties due to variations in temperature. The advantage of this variant is seen, but not restricted to, the use of monitoring cryosurgery.

A system using the modified instrumentation and described methods of the instant invention is capable of producing cross-sectional images of real-time events associated with vascular reactivity in a variety of tissue structures (e.g., limbs, breast, head and neck). Such measurements permit an in-depth analysis of local hemodynamic states that can be influenced by a variety of physiological manipulations, pharmacological agents or pathological conditions. Measurable physiological parameters include identification of local dynamic variations in tissue blood volume, blood oxygenation, estimates of flow rates, and tissue oxygen consumption. It is specifically noted that measurements of several locations on the same medium can be taken. For example, measurements may be taken of the leg and arm areas of a patient at the same time. Correlation of data between the different locations is available using the methods described herein.

The invention also provides both linear and non-linear time series analysis to reveal site specific functionality of the various components of the vascular tree. Thus the response characteristics of the major veins, arteries and structures associated with the microcirculation can be evaluated in response to a range of stimuli.

Fast data collection methods are particularly helpful because there are many disease states with specific influences on the spatial-dynamic properties of vascular responses. Accordingly, it is understood that significantly greater contrast mechanisms are definable, with much greater diagnostic sensitivity. This is accomplished by collecting and evaluating data in the time domain. These results are not available by performing static imaging studies.

The importance of dynamic properties follows directly from an understanding of the well known physiological reactivity of the vascular system. Control of the peripheral vasculature is mediated by neural, humoral and metabolic factors. Neural control is principally through autonomic activity. The details of these properties are well known to many, and can be found in any one of several medical physiology texts. Loss of autonomic control occurs in a variety of disease processes, especially in diabetes. Invariably, this loss of control will adversely influence local perfusion states. The current invention has the capacity to directly evaluate the concept known as vascular sufficiency. This term takes into account the fact that, among its many roles, the vasculature is uniquely responsible for the delivery of essential nutrients to tissue, in particular, oxygen, and for the removal of metabolic waste products. Imbalances between supply and demand lead to relative hypoxic states, which often are clinically significant.

FIG. 1 illustrates one embodiment of the invention. Shown is a system **100** comprising medium **102**. The medium can be any medium in which the propagation of the used source energy is strongly affected by scattering.

From a source module **101** energy is directed to the medium **102** from which the exiting energy is measured by means of detector **106**, further discussed below. As previously discussed, there is a variety of sources, media, and detectors that may be used with the principles of the present invention. The following is a discussion of a sampling of such elements with the intention to describe how the invention is realized. In no way are these examples meant, nor do they intend to limit the invention to these implementations. A variation of elements as described herein may also utilize the principles of the present invention.

In one implementation, measurements of dynamics in the optical properties of the medium is accomplished by using optical source energy and performing rapid detection of the acoustic energy created by absorption processes in the medium. This can be implemented using both pulsed and harmonic modulated light sources, the latter allowing for lock-in detection. Detectors can be, but are not limited to, piezo-electric transducers such as PZT crystals or PVDF foils.

In another variant, a timing and control facility **104** is used to coordinate source and detector operation. This coordination is further described below. A device **116** provides acquisition and storage of the data measured by the detector **106**. Depending on the implementation, control and timing of the system's components is provided by a computer, which includes a central processor unit (CPU), volatile and non-volatile memory, data input and output ports, data and program code storage on fixed and removable media and the like. Each main component is described in greater detail below.

FIG. 2 illustrates another implementation of a preferred embodiment of the present invention. Shown is a system and method that incorporates at least one wavelength measurement. Depending upon the implementation, this measurement is accomplished by alternately coupling light from diode lasers into transmitting fibers arranged in a circular geometry.

Referring again to FIG. 2, a system **200** includes an energy source, which in this implementation includes one or more laser **101**. A reference detector **202** is used to monitor the actual output power of laser **101** and is coupled to a data acquisition unit **116**. Such laser may be a laser diode in the NIR region. The laser is intensity modulated by a modulation means **203** for providing means of separation of background energy sources

such as daylight. The modulation signal is also send to a phase shifter **204** whose purpose is described further below. The light energy generated by the laser **101** is directed into an optical de-multiplexing device **300** further discussed in detail below. Using a rotating mirror **305**, the light is being directed into one of several optical source fiber bundles **306** that are used to deliver the optical energy to the medium **102**. To provide good optical contact and measurement fidelity, one of several possible imaging heads **206** as described further below is used. A motor controller **201** is coupled to the de-multiplexing device **300** for controlling the motion of the rotating mirror **305**. The motor controller **201** is also in communication with a timing control **104** for controlling the timing of the motion of mirror **305**.

The measuring head **206** comprises the common end of a bifurcated optical fiber bundle, whose split ends are formed by the source fiber bundle **306** and detector fiber bundle **207**. Source fiber bundle **306** and detector fiber bundle **207** form a bulls eye geometry at the common end with the source fiber bundle in the center. In other embodiments, source and detector bundles are arranged differently at the common end (e.g., reversed geometry or arbitrary arrangement of the bundle filaments). The common end of a bifurcated optical fiber bundle, preferably comes in contact with the medium, however, this embodiment is not limited to contact with the medium. For example, the common ends may simply be disposed about the medium. The signal is transmitted from the detector fiber bundle **207** to a detector unit **106** that comprises at least one detector channel **205** further described herein.. The detector channel **205** is coupled to the data acquisition unit **116** and the timing control unit **104**. Depending on the implementation, a phase shifter **204** may or may not be used, and is coupled to the detector unit **106** for the

purposes of providing a reference signal for the purposes of filtering the signal received from bundle **207**.

Depending on the implementation, illustrated in FIG. 3 is a device for the measurement of the dynamic properties of a scattering medium. This measurement is performed by sequentially reflecting light **302** off of a rotatable front surface mirror **306**, mounted at a 45 degree angle to the incident source, into source fibers **306** arranged in a circular geometry about the rotating optic. The rotation is done by a motor **308** with a shaft **307** to which the mirror is attached. This embodiment has an advantage of enabling fast switching among the transmitting fibers. In particular, it provides the ability to introduce beam shaping optics between the reflective mirror and transmitting fibers thereby allowing fine adjustment of the illumination area available for coupling into the fibers. This is useful because it allows independent adjustment of the rotation speed of the reflective optic (i.e., switching speed), and the illumination time allowed for each transmitting fiber bundle. Thus, a range of illumination frequencies can be employed while allowing fine adjustment of the illumination time at each source position to permit collection of data having a suitable signal-to-noise ratio.

Light from laser **101** is transmitted to unit **300** by means of transmitting optics **303** including, but not limited to, fiber optics and free propagating beams. Further beam shaping optics **301** may be used to optimize in -coupling efficiency into the transmitting fibers. Units **303** and **301** are under mechanical fine adjustment in their position with respect to the mirror **309**.

Motor **308** is operated under control of motion control **201** to allow for precise positioning and timing. By this means, it is possible to operate the motor under complex

motion protocols such as in a start-stop fashion where the motor stops at a desired location thereby allowing the stable coupling of light into a transmitting fiber bundle. After the measurement at this source location is performed, the motor moves on to the next transmitting fiber. Motion control is in two-way communication with the timing control **104** thereby allowing precise timing of this procedure. Motion control allows the assignment of relative and/or absolute mirror positions allowing for precise alignment of the mirror with respect to the physical location of the fiber bundle. The mirror **306** is surrounded by a cylindrical shroud **309** in order to shield off stray light to prevent cross-talk. The shroud comprises an aperture **310** through which the light beam **302** passes toward the transmitting fiber. It is recognized and incorporated herein other schemes which may be used,(e.g., use of a fiber-optic switching device) to sequentially couple light into the transmitting fibers.

In an equivalent embodiment, fast switching of source positions is accomplished by using a number of light sources, each coupled into one of the transmitting fibers **306** which can be turned on and of each independently by electronic means.

The device employs the servo-motor control system **308** in FIG. 3 with beam steering optics, described above, to sequentially direct optical energy emerging from the source optics onto 1 mm diameter optical fiber bundles **306**, which are mounted in a circular array in the multiplexing input coupler **300**. The transmitting optical fiber bundles **306**, which are typically 2-3 meters in length are arranged in the form of an umbilical and terminate in the imaging head **206**.

Depending on the implementation, the apparatus of the present invention required for time-series imaging, employs the value of using a geometrically adaptive measurement head or imaging head. The imaging head of the present invention provides features that include, but are not limited to, 1) accommodating different size targets (e.g., breast); 2) stabilizing the target against motion artifacts; 3) conforming the target to well-defined geometry; and 4) to provide exact knowledge of locations for sources and detectors. Stability and a known geometry both contribute to the use of efficient numerical analysis schemes.

There are several different embodiments of the imaging head for data collection that may utilize the principles of the present invention. For example the use of an iris imaging head previously disclosed in the '322 and '355 patents , which are incorporated by reference in this disclosure, may be used with the principles of the present invention.

Described below are two exemplary imaging heads with the understanding that the invention may or may not use any type of imaging head, and if an imaging head is used, it would provide the features previously described.

As illustrated in FIG. 4, the iris unit can be employed as a parallel array of irises **402, 404, 406** enabling volume imaging studies. FIG. 4 illustrates how this can be configured for studying a medium **410**, in this example a human breast, using an imaging head **408**. As described previously, the medium used in the present invention can be any medium, which allows scattering of energy.

In one implementation of the imaging head illustrated in FIG. 5, is a flexible pad configuration. This planar imaging unit functions as a deformable array and is well suited to investigate body structures too large to permit transmission measurements (e.g.,

head and neck, torso, and the like). Using this type of imaging head, optical measurements are made in a back-reflection mode. Optical fiber bundles **502** originating from the optical multiplexing input coupler **112** (described elsewhere) terminate at the deformable array or flexible pad **500**. The pad can be made of any flexible material such as black rubber or the like. The optical fiber bundles may be bifurcated and have ends **504** that both transmit and receive light. More than one pad may or may not be used, although an additional pad is not necessary for the purpose of the present invention, or for measurement application to other portions of the medium or to the same medium. For example, in the case of a breast exam, both pads maybe applied to the same breast having one pad above and one pad below the breast. In addition, one pad maybe applied to the right breast by having the pad deformed around the breast. Similarly, the other pad may be applied to the left breast. This configuration would allow both breasts to be examined at the same time. In addition, information may be correlation between the data collected from the two different members of the body. Again, the invention can be applied to other media and is not limited to portions of the human body. Thus, correlation between different media may be collected using this technique.

As further shown in Figure 5, the additional pad would have similar functions as the pad previously described and would have optical fiber bundles **503**, flexible pad **505**, and bifurcated optical fiber bundle ends **501** similar to the previous pad described. The array itself can be deformed to conform to the surface of a curved medium to be imaged (e.g. portion of the torso). The deformable array optical energy source and receiver design includes, depending on the implementation, a 7 x 9 array (63 total bundles) of optical fiber bundles as illustrated in FIG 6. In one variant, each bundle is typically 3

mm in diameter. Depending on the implementation, eighteen (18) of the sixty-three (63) fiber bundles may be arranged in an array to serve as both optical energy sources or energy transmitters, and receivers to sequentially deliver light to a designated target and receive emerging optical energy. In this implementation, the remaining forty-five (45) fiber bundles act only as receivers of the emerging optical energy.

The geometry of the illumination array is not arbitrary. The design shown in Figure 6 as an exemplary illustration has been configured, as have other implementations, to minimize the subsequent numerical effort required for data analysis while maximizing the source-density covered by the array. The fiber bundles are arranged in an alternating pattern as described by FIG. 6 and shown here with the symbols "X" and "0". In one implementation, a pattern of 00X000X00, X000X000X can be used on the imaging head. 'X' denotes a source/receiver fiber bundle, and '0' is a receiver only a receiver or detector fiber bundle. Basically, the design allows for the independent solution of two dimensional (2-D) image recovery problems from an eighteen (18) point source measurement. As a result, a composite three dimensional (3-D) image can be computed from superposition of the array of 2-D images oriented perpendicular to the target surface. Another advantage of this geometry is that it readily permits the use of parallel computational strategies without having to consider the entire volume under examination.

The advantage of this geometry is that each reconstruction data set is derived from a single linear array of source-detector fibers, thereby enabling solution of a 2-D problem without imposing undue physical approximations. The number of source-detector fibers belonging to an array can be varied. Scan speeds attainable with the 2-D array illustrated in FIG 6 are the same as for other imaging heads with 2-D arrays since

the scan speed depends only on the properties of the input coupler. Thus, faster scan speed are available for the creation of a 3-D image.

In another implementation, illustrated in FIG. 7, is an imaging head based on a "Hoberman" sphere geometry. In a Hoberman structure, the geometry is based on the intersection of a cube and an octahedron, which makes a folding polyhedron called a trapezoidal icosatetrahedron. This structure has been modified and implemented in a form of an imaging head of a hemispherical geometry. For many purposes of the instant invention, it is appropriate to use design features of smoothly varying surfaces based on the Hoberman concept of expanding structures. Depending on the implementation, other polygonal or spherical-type shapes may also be used with the principles of the present invention for other imaging head designs. Adjustment of the device in Figure 7 causes uniform expansion or contraction, thereby always preserving a hemispherical geometry. Imaging head **700** illustrates one example of modification to the "Hoberman" geometry. A receptacle for the fiber bundles **701** is disposed about imaging head **700**. Target volume **702** is where the medium would enter the imaging head in this implementation. This geometry is well suited for the investigation of certain tissues such as the female breast or the head. Depending on the implementation, attachment of optical fibers to the vertices of the hemisphere allows for up a seventeen (17) source by seventeen (17) detector measurement. The detectors or energy receivers may be disposed about the spherical imaging head and the detectors are located on the inner aspect of the expanding imaging head. Additional fiber bundles can be attached to the interlocking joints, permitting up to a 49 source by 49 detector measurement.

Depending on the implementation, light collected from the target medium is measured by using any of a number of optical detection schemes. One embodiment uses a fiber-taper, which is bonded to a charged coupled detector (CCD) array. The front end of the fiber taper serves to receive light exiting from the collection fibers. These fibers are preferably optical fibers, but can be any means that allows the transmission and reception of signals. The back end of the fiber taper is bonded to a 2-D charge-coupled-detector (CCD) array. In practice, use of this approach generally will require an additional signal attenuation module.

An alternate detection scheme employs an array of discrete photo detectors, one for each fiber bundle. This unit can be operated in a phase lock mode thereby allowing for improved rejection of ambient light signals and the discrimination of multiple simultaneously operated energy sources.

In another embodiment, in order to fulfill the demands posed by the desired physiological studies on the instrument, the following features characterize the detector system: scalable multi-channel design (up to 32 detector channels per unit); high detection sensitivity (below 10 pW); large dynamic range ($1{:}10^6$ minimum); multi-wavelength operation; ambient light immunity; and fast data acquisition (order of 100 Hz all-channel simultaneous capture rate).

To achieve this, the detector system uses photodiodes and a signal recovering technique involving electronic gain switching and phase sensitive detection (lock-in amplification) for each detector fiber (in the following referred to as detection or detector channels) to ensure a large dynamic range at the desired data acquisition rate. The phase sensitive signal recovery scheme not only suppresses electronic noise to a desired level

but also eliminates disturbances given by background light and allows simultaneous use of more than one energy source. Separation of signals from simultaneously operating sources can be achieved, as long as the different signals are encoded in sufficiently separated modulation frequencies. Since noise reduction techniques are based on the reduction of detection bandwidth, the system is designed to maintain the desired rate of measurements. In order to achieve a timing scheme that allows simultaneous readout of the channels, a sample-and-hold circuit (S/H) is used for each detection channel output. The analog signals provided by the detector channels are sampled, digitized and stored using the data acquisition system **116**. One aspect is the flexibility and scalability of the detection instrument. Not only are the detector channels organized in single, identical modules, but also the phase detection stages, each containing two lock-in amplifiers, are added as cards. In this way, an existing setup can easily be upgraded in either the number of detector channels and/or the number of wavelengths used (up to four) by cloning parts of the existing hardware.

FIG. 8 shows the block diagram of one implementation of a detector channel. In this implementation , two energy sources are being used. After detecting the light at the optical input **801** by a photo detector **802** the signal is fed to a transimpedance amplifier **803**. The transimpedance value of **803** is externally settable by means of digital signals **813** (PTA=Programmable Transimpedance Amplifier). This allows the adaptation to various signal levels thereby increasing the dynamic range of the detector channel. The signal is subsequently amplified by a Programmable Gain Amplifier (PGA) whose gain can be set externally by means of digital signals **814**. This allows for additional gain for

the lowest signal levels (e.g., in one implementation ~pW-nW) thereby thereby increasing the dynamic range of the detector channel.

In one embodiment, at least one energy source is used and the signal is sent to at least one of lock-in amplifiers (LIA) **805, 809**. Each lock-in amplifier comprises an input **808,812** for the reference signal generated by phase shifter **204** from FIG 2. After lock-in detection, the demodulated signal is appropriately boosted in gain by means of a programmable gain amplifier (PGA) **806, 810** in order to maximize noise immunity during further signal transmission and to improve digital resolution when being digitized. The gain of PGA **806, 810** is set by digital signals **815**.

At each output, a sample-and-hold circuit (S/H) **807, 811** is used for freezing the signal under digital timing by means of signal **816** for purposes described herein.

In one embodiment, the signal **815** is sent to **806, 810** in parallel. In one embodiment, the signal **816** is sent to **807, 811** in parallel.

As previously illustrated in FIG. 1, the analog signal provided by each of the channel outputs is sampled a data acquisition system **116**. In one embodiment, PC extension boards might be used for this purpose. PC extension boards also provide the digital outputs that control the timing of functions such as gain settings and sample-and-hold.

As previously noted, timing is crucial in order to provide the desired image capture rate and to avoid false readings due to detector-to-detector time skew. FIG. 9 shows one improvement of the invention over other timing schemes. With systems not comprising fast adaptable gain settings (such as some CCD based systems), a schedule according to **905** has to be implemented. The implementation in FIG 9 illustrates one use

of a silicon photo-diode in process **904**, which can be replaced by various detectors previously mentioned. A time series of data is acquired for a fixed source position. After finishing this task, the source is being moved **902** with respect to the target **901** and another series of data is being collected. Measurements are being performed in this fashion for all source positions. Every image **903** of the resulting time series of reconstructed images are being reconstructed from data sets merged together from the data for each source position. This schedule does not allow real-time capture of all physiologic processes in the medium and therefore only applies to certain modes of investigation. Although we are aware of the use of such schemes, e.g., when monitoring responses on repeatable maneuvers, the timing scheme for the invention very much improves on this situation.

Because the invention allows for fast source switching and large dynamic range and high data acquisition rates, a schedule indicated by **904** is performed. Here, the source position is switched fast compared to the dynamic features of interest and instantaneous multi-channel detection is performed at each source position. Images **903** are then reconstructed from data sets, which represent an instant state of the dynamic properties of the medium. Only one time series of full data sets (i.e., all source positions and all detector positions) is being recorded. Real time measurement of fast dynamics (e.g., faster 1 Hz) of the medium is provided by the invention.

FIG 10 shows one embodiment of a detailed schedule and sequence of the system tasks **1001** involved in collecting data at a source position and the proceeding of this process in time **1002**. Task **1003** is the setting of the optical de-multiplexer to a destined source position and setting the detectors to the appropriate gain settings. The source

position is illuminated for a period of time **1004**, during which the lock-in amplifiers settle **1005**. After the time it takes the S/H to sample the signal **1006**, the signal is being hold for a period of time **1007**, during which all channels are being read pout by the data acquisition. It is worthwhile noticing that during reading out the S/H, other tasks, like moving the optical source, setting the detector gains for the new source position, and settling of the lock-in, are being scheduled. This increases greatly the achievable data acquisition rate of the instrument.

This concept of a modular system is further illustrated in FIG. 11. Up to thirty-two (32) detector modules **1100** (each with 2 lock-in modules each for two modulation frequencies) are arranged using an enclosure **1102**. The cabinet also can carry up to two phase shifting modules **1104**, **1106**, each containing two digital phase shifter under computer control. The ability to adjust the reference phase with respect to the signal becomes necessary since unavoidable phase shifts in the signal may lead to non-optimum lock-in detection or can even result in a vanishing output signal. Organization of data, power supply and signal lines is provided by means of two back planes **1108**, **1110**

Depending on the implementation, the detector system design illustrated in FIG. 8 allows one cabinet to operate at a capacity of 32 detectors with four different sources requiring 128 analog to digital circuit (ADC)-board input channels. The upper **1108** and the lower **1110** back plane are of identical layout and have to be linked in order to provide the appropriate distribution of supply-, control- and signal voltages. This is achieved using a 6U-module fitting both planes from the backside, that provides the necessary electric linking paths, and interfaces for control- and signal lines.

FIG. 12 shows the schematic of one implementation of a channel module. In this implementation, a silicon photodiode 1206 is used as the photo-detector. A Programmable Transimpedance Amplifier (PTA) **1201** is formed by an operational amplifier **1204** , resistors **1201** and **1202** and an electronic switch **1205**, the latter of which is realized using a miniature relay. Other forms of electronic switches such as analog switches might be used. Relay **1205** is used to connect or disconnect 1203 from the circuit thereby changing the transimpedance value of **1201**. A high-pass filter (R2, C5) is used to AC-couple the subsequent programmable gain instrumentation amplifier **IC2** (Burr Brown PGA202) in order to remove DC offset. The board-to-board connectors for the two lock-in-modules are labeled as "slot A" **1210** and "slot B" **1212**. The main connector to the backplane is a 96-pole DIN plug **1220**.

FIG. 13, illustrates the electric circuit of the lock in modules **1210, 1212**. The signal is subdivided and passed to two identical lock-in-amplifiers, each of which gets one particular reference signal according to the sources used in the experiment. The signal is first buffered **IC1, IC7** (AD LF111) and then demodulated using an AD630 double-balanced mixer **IC2, IC8**.

In order to remove undesired AC components, the demodulated signal passes through an active 4-pole Bessel-type filter **IC3, IC4, IC 9, IC10** (Burr Brown UAF42). A Bessel-type filter has been chosen in order to provide fastest settling of the lock-in amplifier for a given bandwidth. Since a Bessel-filter shows only slow stopband-transition, a 4-pole filter is being used to guarantee sufficient suppression of cross talk between signals generated by different sources (i.e. of different modulation frequency). The filter has its 3 dB point at 140 Hz, resulting in 6 ms settling time for a step response

(<1% deviation of actual value). The isolation of frequencies separated by 1 kHz is 54 dB. The filters are followed by a programmable gain amplifier **IC5, IC 11**, whose general function has been described above. The last stage is formed by a sample-and-hold chip (S/H) **IC6, IC12** (National LF398).

In another implementation, the phase sensitive detection can be achieved with digital methods using digital signal processing (DSP) components and algorithms. The advantage of using DSP with the principles of the present invention is improved lectronic performance and enhanced system flexibility.

In another implementation, an analog-to-digital converter is used for each detector channel thereby improving noise immunity of the signals.

Although illustrative embodiments have been described herein in detail, those skilled in the art will appreciate that variations may be made without departing from the spirit and scope of this invention. Moreover, unless otherwise specifically stated, the terms and expressions used herein are terms of description and not terms of limitation, and are not intended to exclude any equivalents of the system and methods set forth in the following claims.

What is claimed is:

1. A system for use in tomographic imaging of a scattering medium, comprising:

an energy source for emitting a signal and having at least one energy transmitter coupled thereto; and

a detection system coupled to the energy source and including at least one energy receiver for measuring dynamic properties of the scattering medium.

2. The system of claim 1, further including an imaging head coupled as the energy transmitter and energy receiver for holding thereof.

3. The system of claim 1, wherein the detection system further comprises at least one lock-in amplifier for separating a signal emitted by at least one energy source.

4. The system of claim 1, wherein the detection system further includes at least one gain adjustment means for increasing dynamic range of the detector system.

5. The system of claim 1, wherein the detection system further includes a sample-and-hold circuit for freezing the signal emitted by the energy source.

6. The system of claim 5, wherein the sample-and-hold circuit further includes logic for allowing simultaneous readout for each detector fiber.

7. The system of clam 1, wherein the energy source includes at lest one of non-laser optical sources, LED and high-pressure incandescent lamp, laser diodes, solid state lasers, titanium-sapphire laser, ruby laser, dye laser, electromagnetic sources, acoustic energy, acoustic energy produced by optical energy, optical energy, and combinations thereof.

8. The system of claim 1, wherein data acquisition from the detection system is about 150Hz.

9. The system of claim 1, wherein the energy source includes a plurality of near infra red laser diodes to transmit multiple wavelengths.

10. A detection system to collect data about the dynamic properties of a scattering medium, comprising:

at least one energy receiver for detecting a signal from an energy source; and

a programmable gain instrumentation amplifier for increasing the dynamic range of the signal which provides rapid data acquisition about the dynamic properties of the scattering medium.

11. The detection system of claim 10, wherein the energy receiver includes at least one of a photo-diode, PIN diode, Avalanche photodiodes , change couple device, change inductive device, photo-multiplier tubes, multi-channel plate, acoustic transducers, and any combinations thereof.

12. The detection system of claim 10, further including a sample-and-hold circuit coupled to the programmable gain instrumentation amplifier that allows simultaneous readout of a plurality of signals from the energy source.

13. A system for use in optical tomographic imaging of a scattering medium comprising:

at least one energy transmissive fiber bundle coupled to an energy source;

an imaging head for holding the energy transmissive fiber bundle; and

a detection system for collecting data about the optical dynamic properties of the scattering medium.

14. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

15. The system of claim 13, wherein the fiber bundle is bifurcated to both transmit and detect energy.

16. The system of claim 13, wherein the imaging head is a folding sphere or polygon.

17. The system of claim 16, wherein the polygon is a polyhedron or a trapezoidal icosatetrahedron, or a hemitrapezoidal icosatetrahedron..

18. The system of claim 16, wherein the fiber bundle is disposed about the imaging head.

19. The system of claim 13 wherein the fiber bundle has a diameter of about 3 mm.

20. The system of claim 13, wherein the imaging head further includes adjustment means for accommodating different size medium, stabilizing the medium against motion artifacts, conforming the target to a simple well-defined geometry and

providing information about the location of at lest the receiver in reference to the location of the transmitter.

21. A method of using optical tomographic imaging, comprising:

(a) exposing a scattering medium to near infra-red light; for collecting data about the dynamic properties of a scattering medium,

(b) detecting light by a detection system; and

(c) enhancing gain through a programmable gain instrumentation amplifier for the purpose of measuring the dynamic properties of the scattering medium.

22. The method of claim, wherein the scattering medium is vascular tissues.

23. The method of claim 21, further including separating via at least one lock-in amplifier a plurality of wavelengths transmitted through the medium.

24. The method of claim 21, further including collecting data from simultaneous readouts of a signal.

25. A system for optical tomographic imaging of a medium comprising:

an imaging head having at least one source disposed to direct optical energy into a medium and a plurality of detectors disposed to receive optical energy emerging from the medium, the detectors means being located at a plurality of distances from the source constituting a plurality of distances through the medium the detectors and thee source , the source and detectors forming respective source detector pairs;

a programmable gain amplifier connected to amplify at least one signal of the source detector pairs;

a computer having a data acquisition board for receiving the signal from the programmable gain amplifier and reconstructing an image of the medium.

26. The system of claim 25, wherein the optical energy comprises optical energy of at least two different intensity modulated wavelengths of energy.

27. The system of claim 26, further comprising a filtering means for separating signals corresponding to a wavelength of intensity modulated energy.

28. The system of claim 25, further comprising a sample and hold circuit for holding a desired signal for use in measuring of dynamic properties of the medium.

29. The system of claim 25, wherein the source comprises energy transmissive fibers coupled to an energy emitting source.

30. The system of claim 25, wherein the source comprises a plurality of optical energy sources.

31. The system of claim 25, wherein the source comprises of plurality of laser diodes.

32. The system of claim 25, wherein the detectors are fibers coupled to optical energy detectors.

33. The system of claim 25, wherein the detectors are optical energy detectors.

34. An imaging head comprising

a pad;

a plurality of source means for delivering optical energy to a medium; and

a plurality of detector means for detecting optical energy emerging from a medium, the source means and detector means being attached to the pad in a plurality of rows and columns wherein the plurality of source means are arranged to form at least two unique imaging planes, an imaging plane being between defined by a plane substantially perpendicular to the pad and passing through at least two source means and one detector means.

35. The imaging head of claim 34, wherein a plurality of source means and detector means are joined to form combined source detector means, the combined source detector means and detector means being arranged in an alternating rows of a first pattern and a second pattern, the first pattern comprising one combined source detector means followed by three detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means, the second pattern comprising two detector means followed by one combined source detector means followed by three detector means followed by one combined source detector means followed by two detector means.

36. The imaging head of claim 34, wherein the source means are fibers coupled to an optical energy source.

37. The imaging head of claim 34, wherein the source means are optical energy sources.

38. The imaging head of claim 34, wherein the source means is laser diodes.

39. The imaging head of claim 34, wherein the detector means are fibers coupled to optical energy detectors.

40. The imaging head of claim 34 wherein the detector means are optical energy detectors.

41. The imaging head of claim 34 wherein the detector means are photodiodes.

42. An adjustable imaging head of folding polyhedron structure defined by a plurality of scissors pairs having identical rigid angulated truss elements, each trust element having a central pivot point, an internal terminal pivot point and an external terminal pivot point that do not lie on a straight line, each strut being pivotally joined to the other of its pair by their central pivot points, each strut being pivotally joined by the internal terminal pivot point and the external terminal pivot point to the internal terminal pivot point and the external terminal pivot point respectively of another scissors pair, whereby an adjustable ring of principle vertices is formed by the internal terminal pivot points and whereby adjustment causes uniform movement of the principle vertices, the improvement comprising:

at least one source means for delivering optical energy into a medium and at least one detector means for detecting optical energy emerging from a medium, wherein the source means and the detector means are attached to the principle vertices, the source means being oriented to direct optical energy substantially toward a medium in

the center of the ring, the detector means being oriented to receive optical energy emerging substantially from a medium in the center of the ring.

43. The adjustable imaging head of claim 42, further comprising:

amount in communication with a truss element, wherein the mount supports the imaging head and regulates the size of the adjustable ring.

44. The adjustable imaging head of claim 42, further comprising:

a first set of mounts in communication with a first set of diametrically opposed external terminal pivot points;

a second set of mounts in communication with a second set of diametrically opposed external terminal pivot points, wherein the first set of diametrically opposed external terminal pivot points is orthogonal to the second set of diametrically opposed external terminal pivot points,

a drive system in communication with at least one of the mounts in at least one of the first or second sets of mounts, whereby the drive system regulates the size of the adjustable ring.

45. The imaging head of claim 42, wherein the source means are fibers coupled to an optical energy source.

46. The imaging head of claim 42, wherein the source means are optical energy sources.

47. The imaging head of claim 42, wherein the source means are laser diodes.

48. The imaging head of claim 42, wherein the detector means are fibers coupled to optical energy detectors.

49. The imaging head of claim 42, wherein the detector means are optical energy detectors.

50. The imaging head of claim 42, wherein the detector means are photodiodes.

51. An imaging head for use in optical tomography, comprising:

at least one energy receiver;

adjustment means for accommodating different sizes of the medium; and

communication means for transmitting signals from the imaging head to a detection system for use in the measurement of dynamic properties of a scattering medium.

52. The imaging head of claim 49, further including at least one energy transmitter.

53. The imaging head of claim 52, wherein the energy transmitters define an illumination array configured to minimize subsequent numerical effort required for data analysis and maximizing source density covered by the array.

54. The imaging head of claim 53, wherein three dimensional images can be computed from super positioning of the array of two dimensional images.

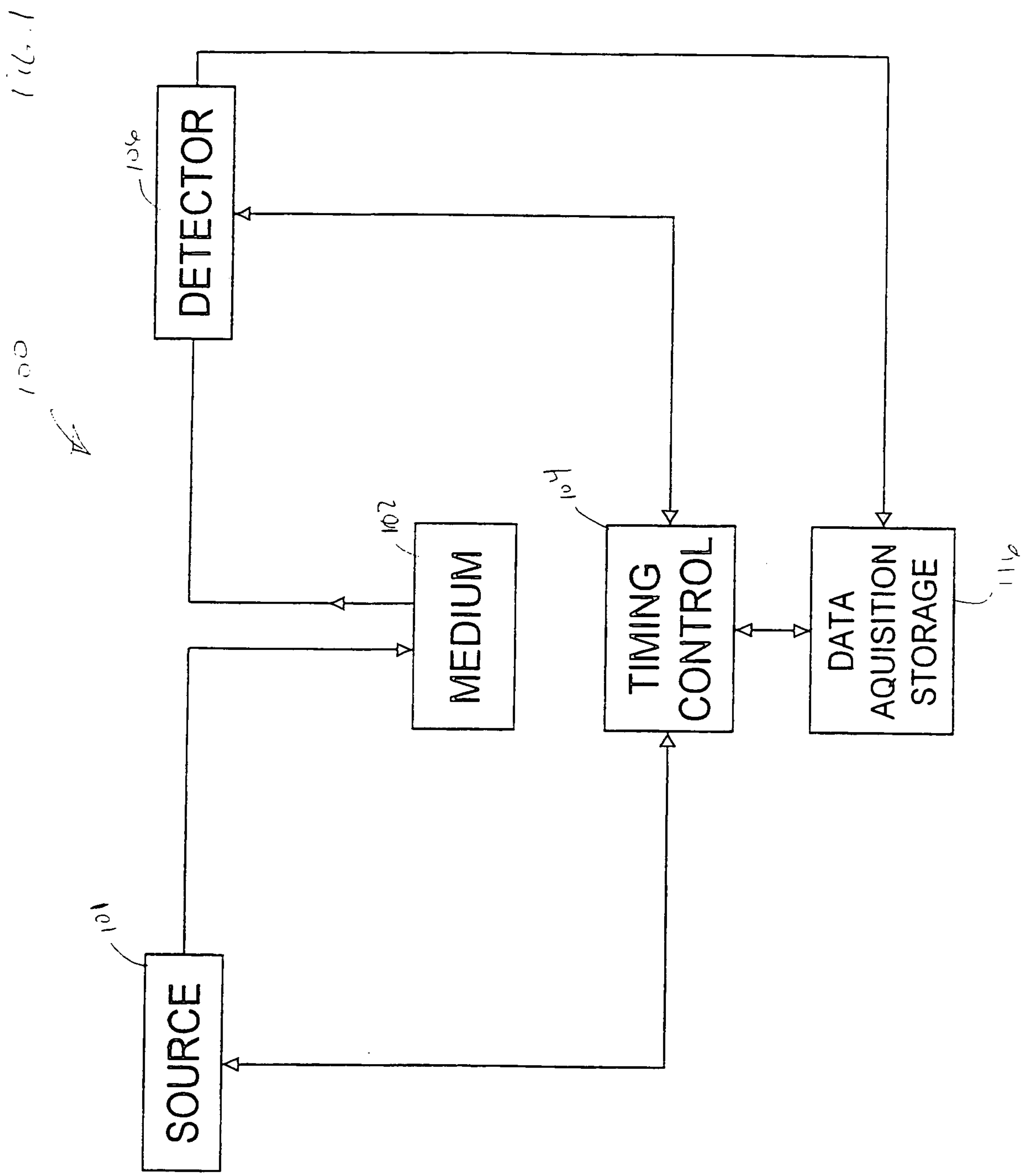

DETECTOR
MEDIUM
SOURCE
TIMING
CONTROL
DATA
AQUISITION
STORAGE

FIG. 2

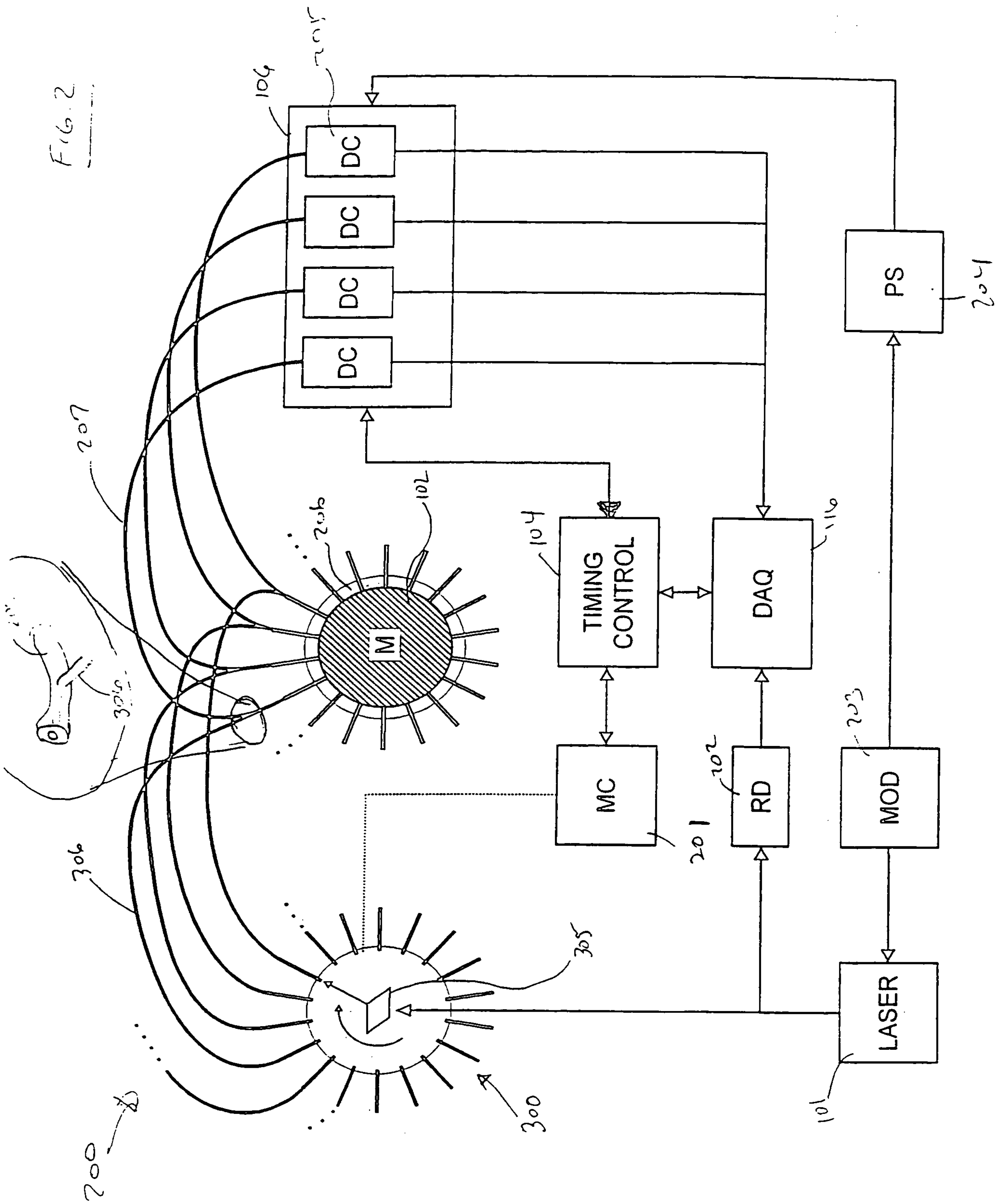
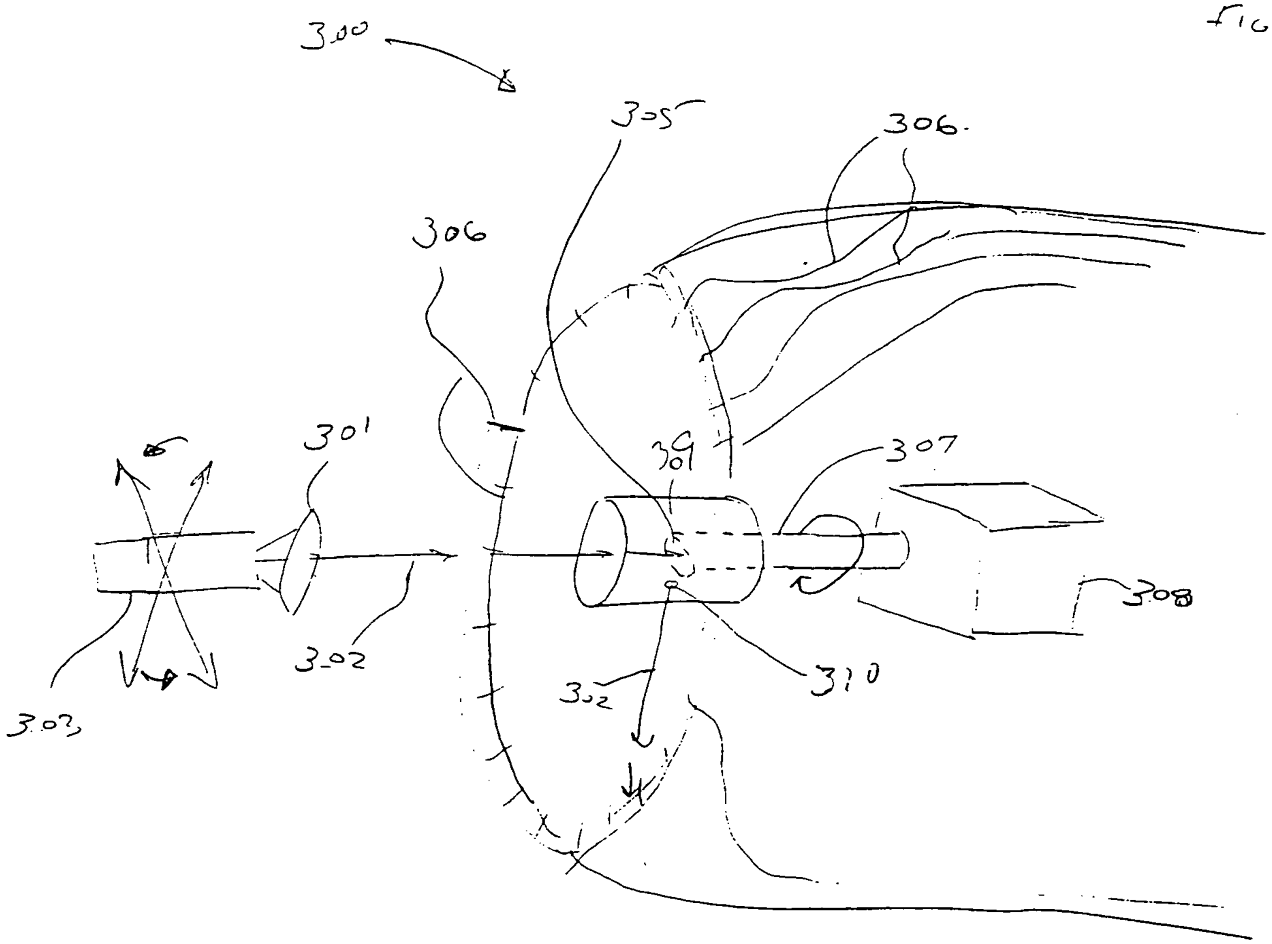

DC
DC
DC
DC
PS
TIMING CONTROL
DAQ
M
MC
RD
MOD
LASER
104
205
207
102
206
104
116
204
201
202
203
306
305
300
101
200

FIG 3



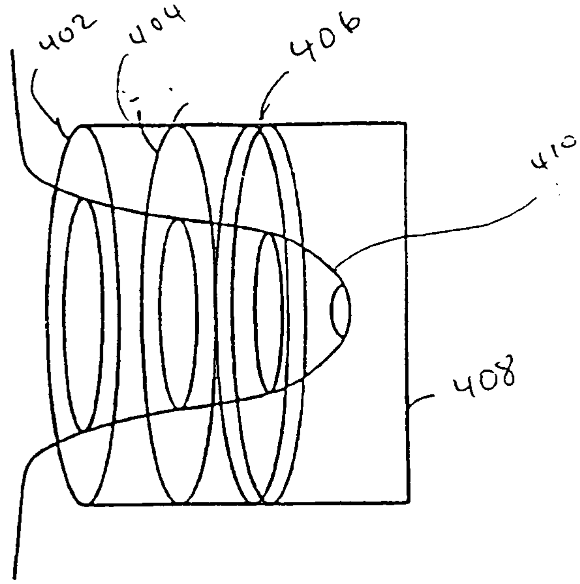


FIG 4

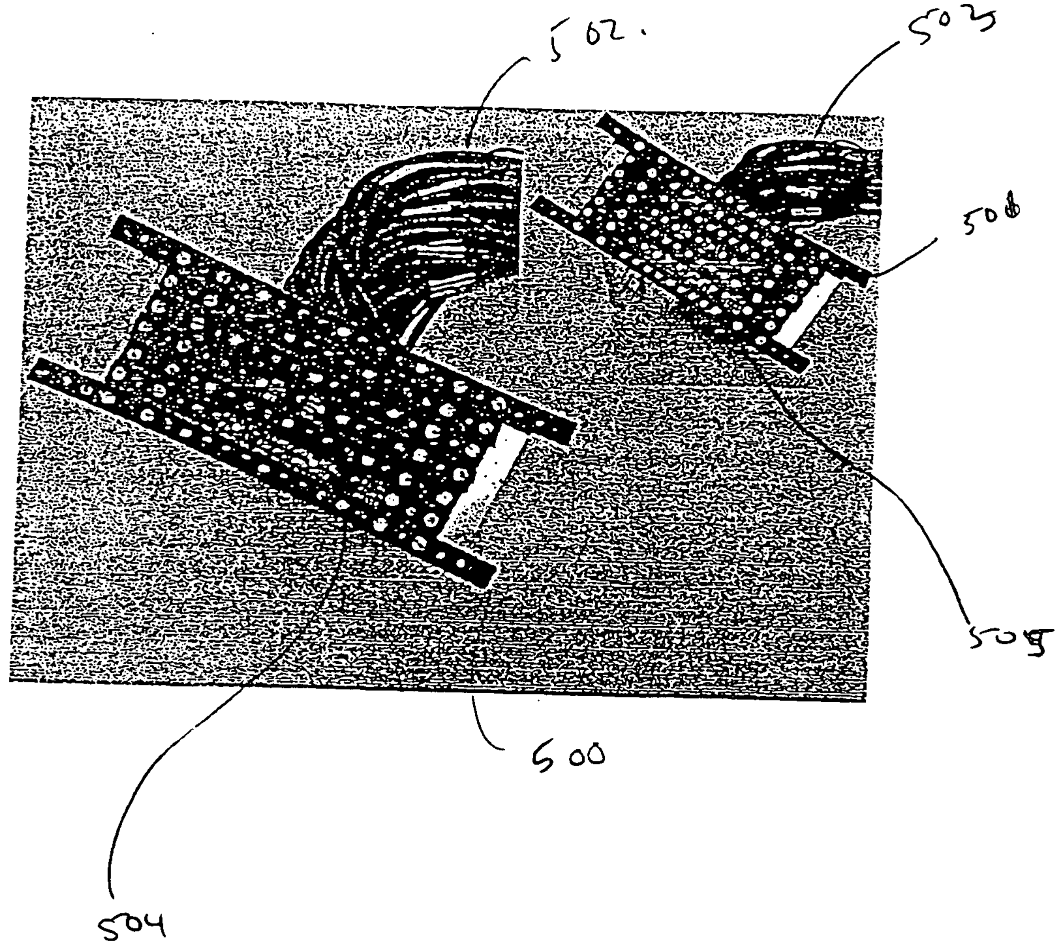


FIG 5

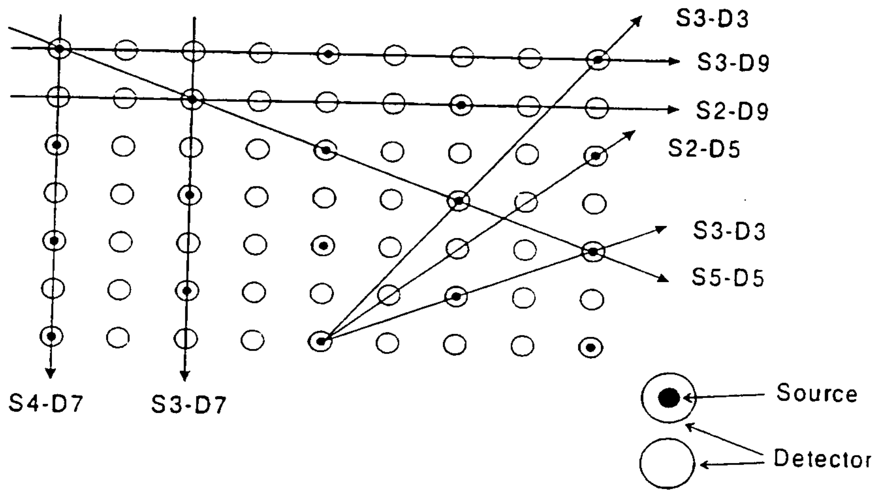


Figure 6

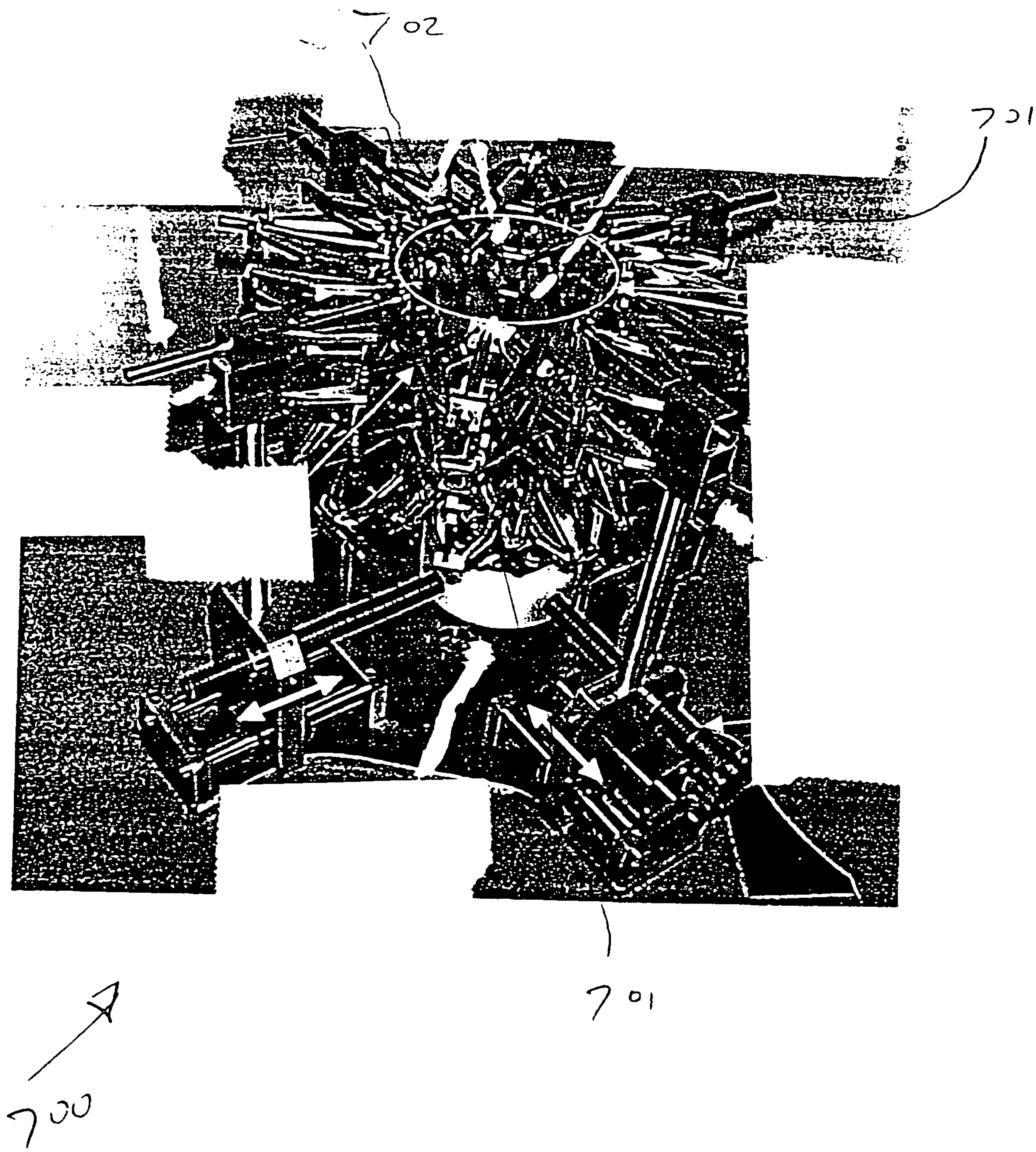


Figure
7

JC13 Rec'd PCT/PTC 14 MAR 2002

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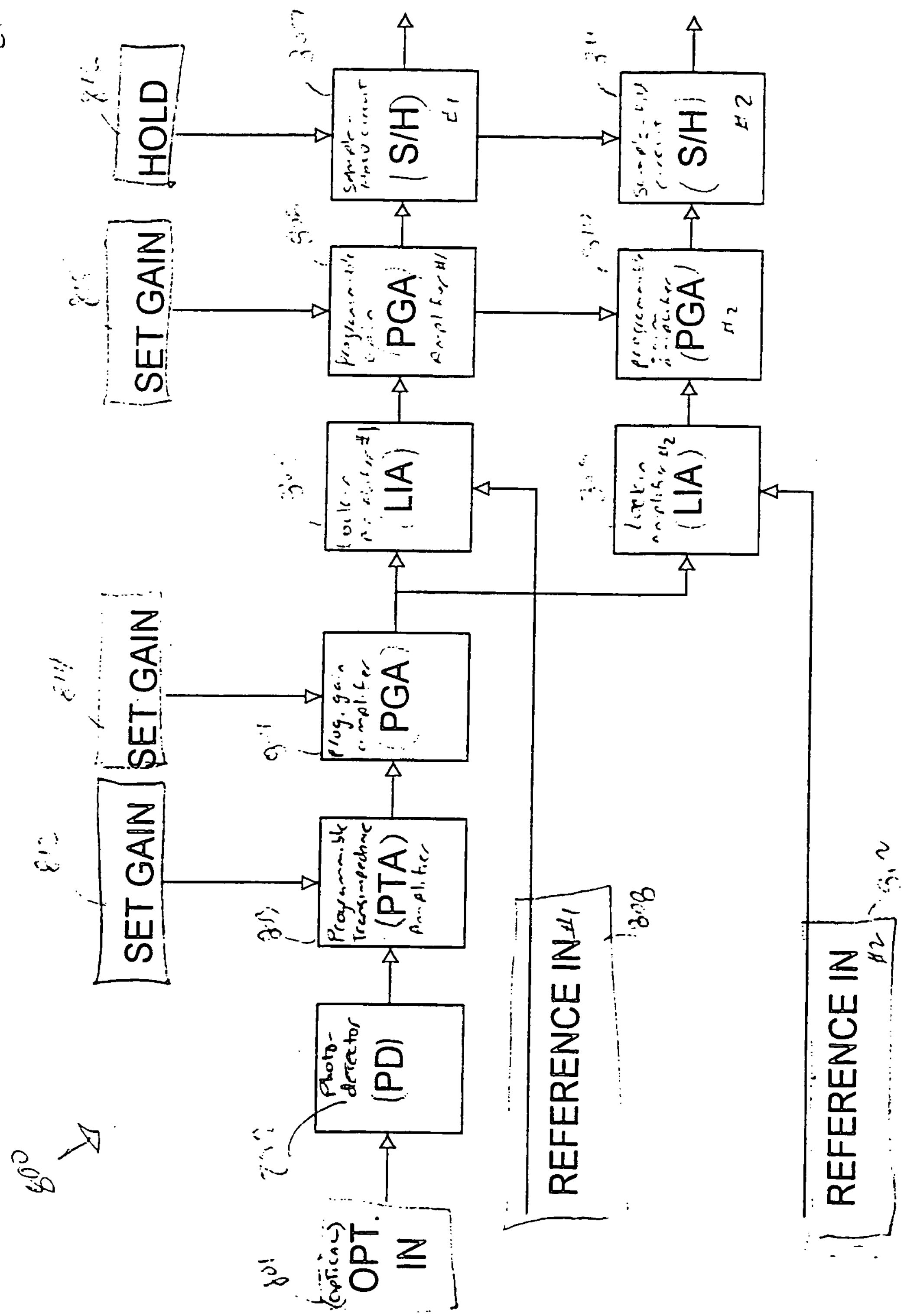
10/088254

FIG 8



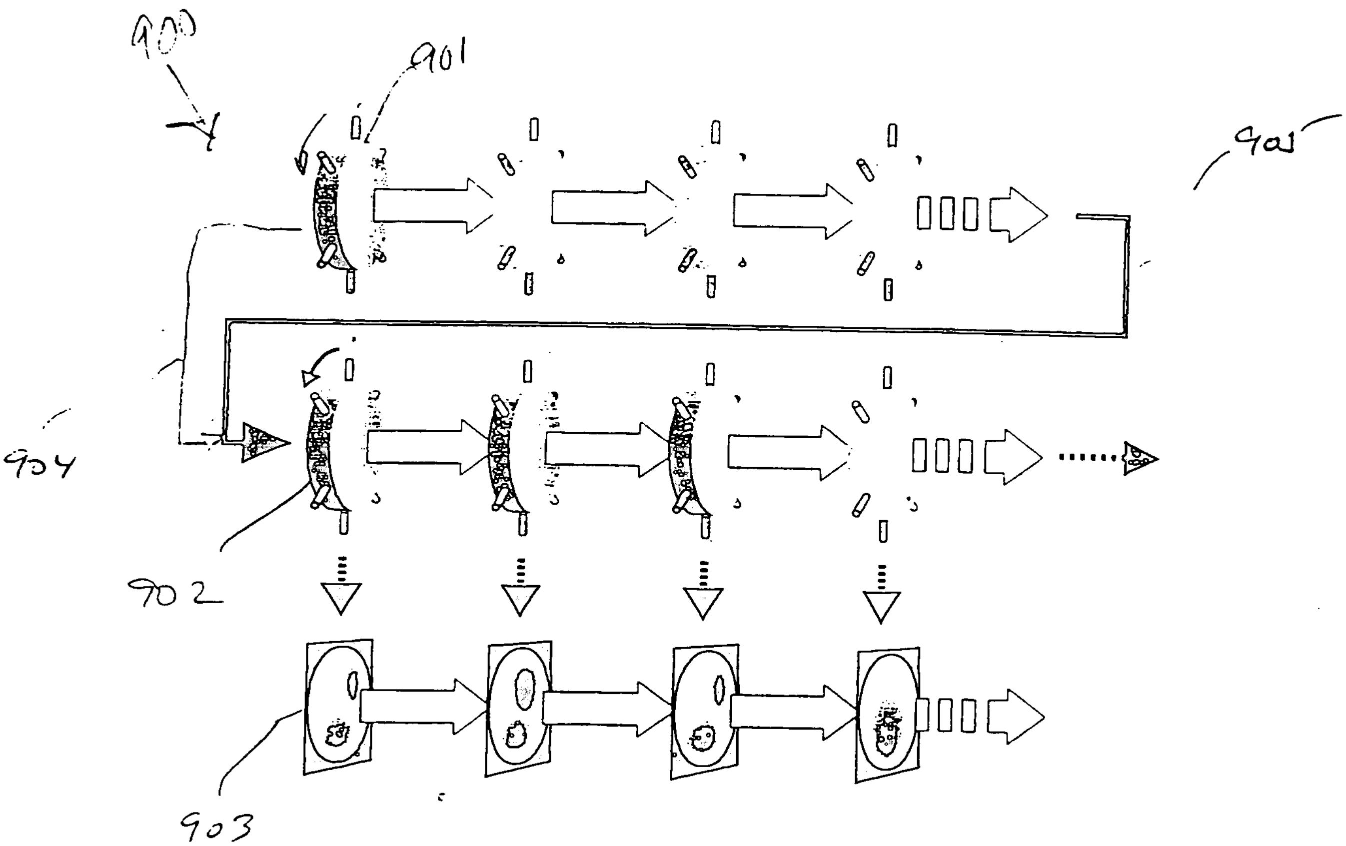


FIG 9

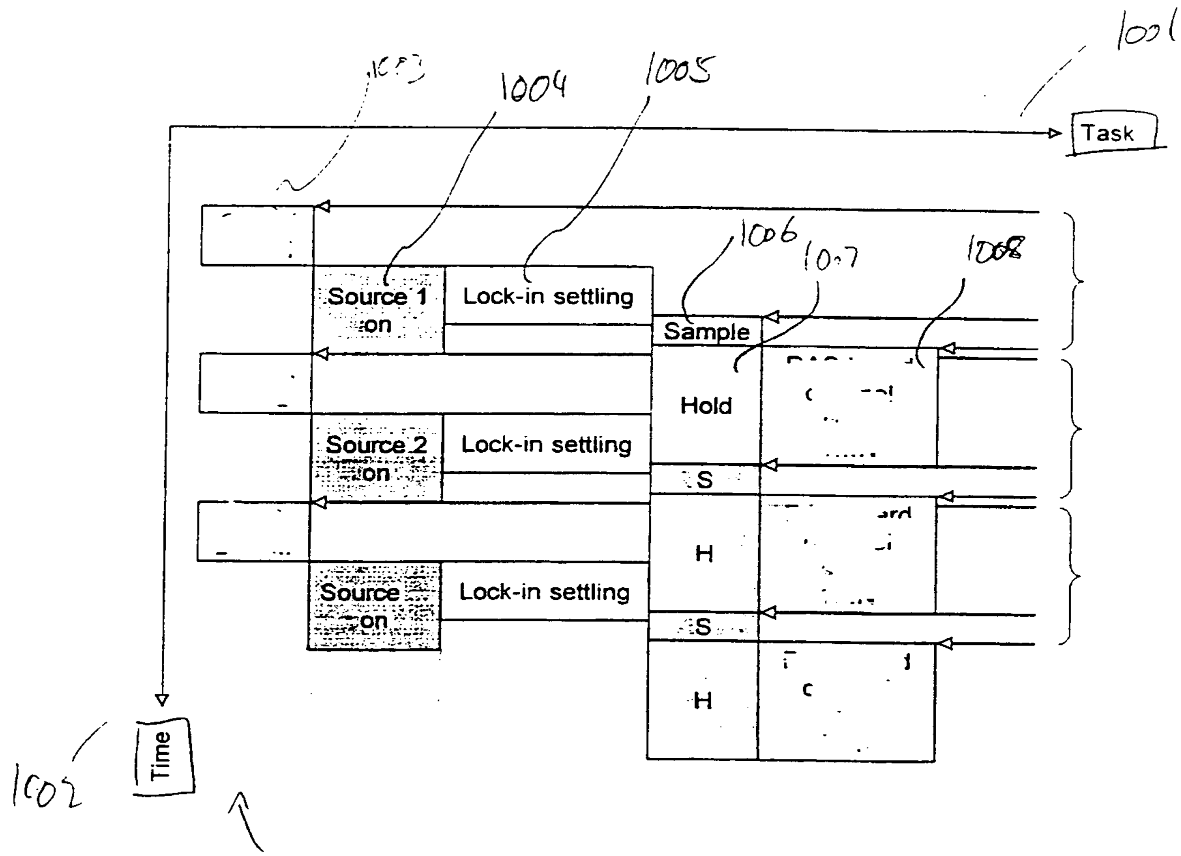

1001
1003
1004
1005
Task
1006
1007
1008
Source 1 on
Lock-in settling
Sample
Hold
Source 2 on
Lock-in settling
S
H
Lock-in settling
S
H
Time
1002

FiG 10

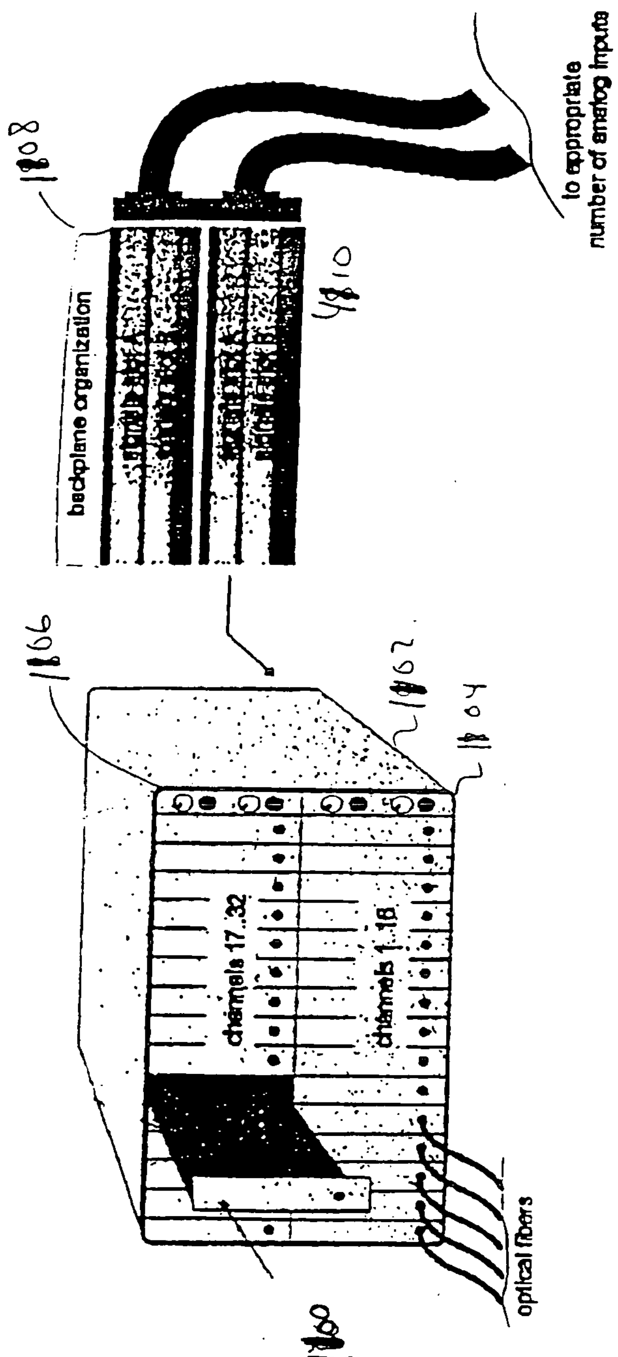
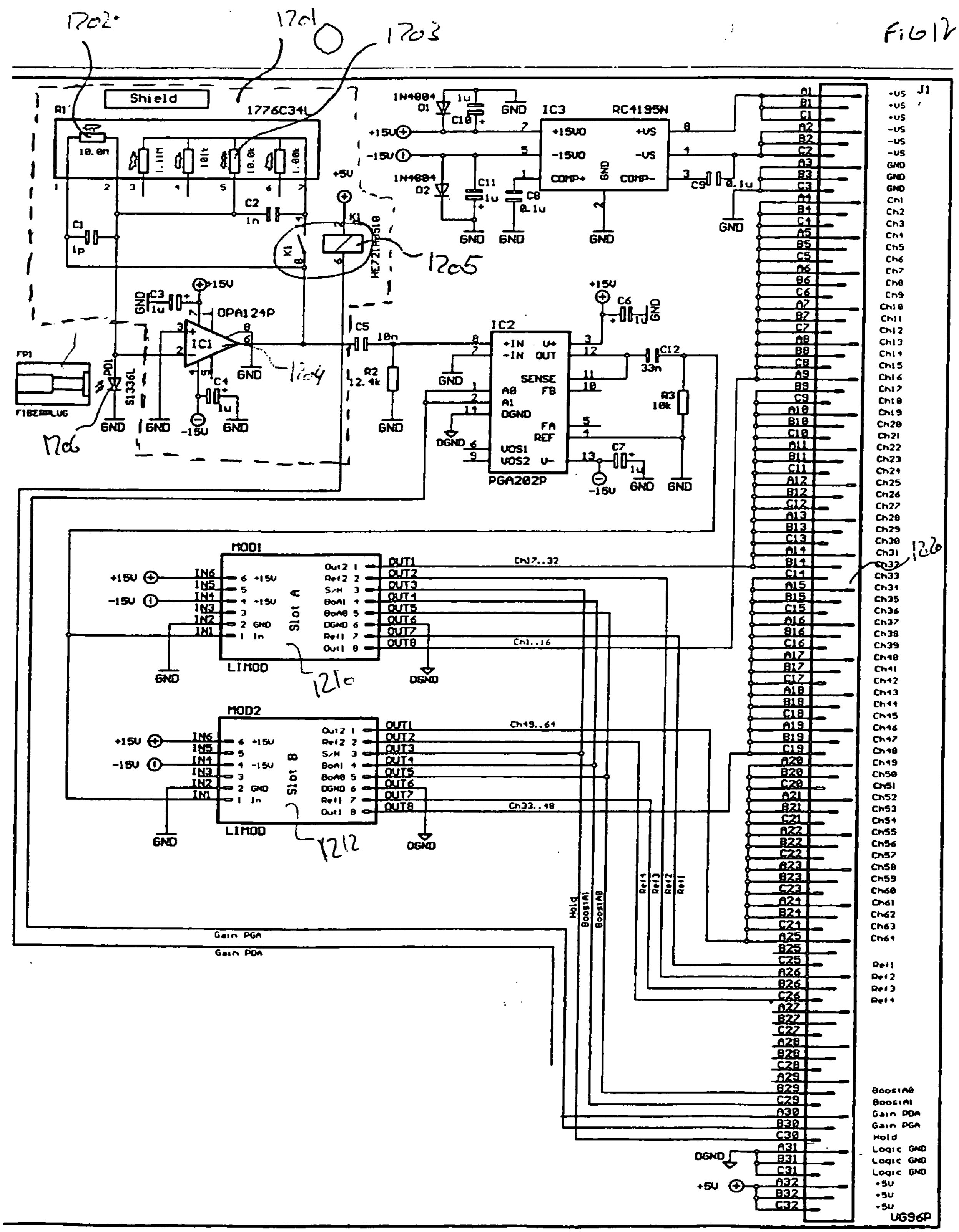
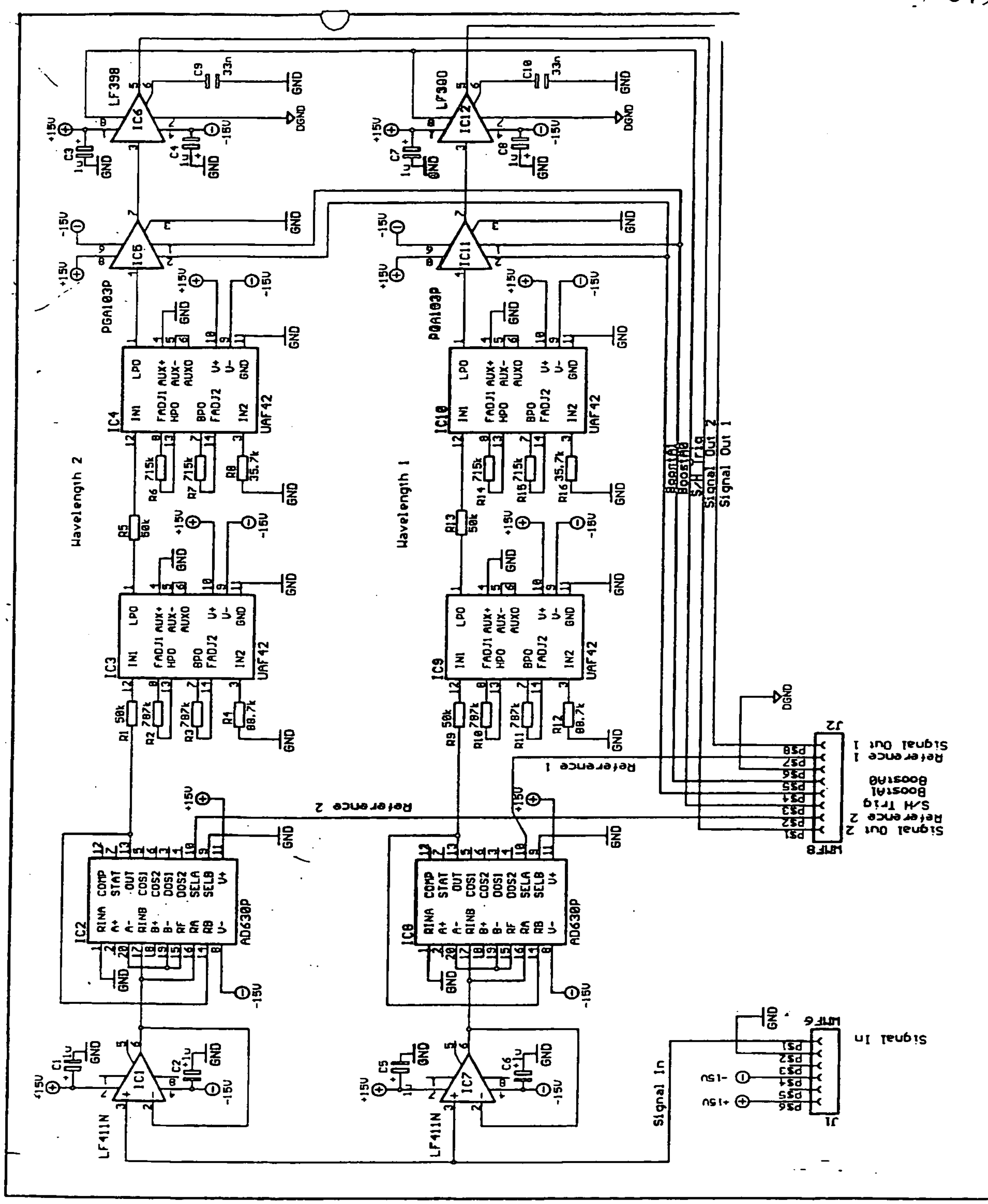

1808
backplane organization
1810
to appropriate
number of analog inputs
1806
1802
1804
channels 17..32
channels 1..16
optical fibers
1800

FIG 11

FIG 12



F 6 13


IC1
IC2
IC3
IC4
IC5
IC6
IC7
IC8
IC9
IC10
IC11
IC12
LF398
PGA103P
UAF42
AD630P
LF411N
Wavelength 2
Wavelength 1
Reference 1
Reference 2
Signal In
Signal Out 1
Signal Out 2
S/H Trig
BoostA1
BoostA0
J1
J2
GND
DGND
+15V
-15V

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/25155

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :G01N 21/00; H01J 3/14
US CL :356/436; 250/216
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 356/436; 250/216

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P ---- A	US 5,994,690 A (Kulkarni et al) 30 November 1999, see entire document.	1-3,7,13,14,19 ----- 4-6,8-12,15-18,20-54

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
02 NOVEMBER 2000	09 JAN 2001

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